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CLINICAL FEATURES AND TREATMENT OF DIAPHRAGMATIC HERNIA

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The literature about the diagnosis and treatment of diaphragmatic hernia is misleading. It puts too much emphasis on the favorable cases; it stresses insufficiently the poor results due to improper diagnosis or unnecessary treatment. Dramatic results have followed the surgical repair of some diaphragmatic hernias. On the other hand, intractable reflux esophagitis, unfavorable vagal sequelae, and disabling intercostal neuralgia have been seen postoperatively in patients whose diaphragmatic hernias had little or nothing to do with their preoperative complaints.

This paper will briefly review the clinical features of diaphragmatic hernia. It will evaluate the conservative method of treatment and will attempt to clarify the indications for surgical intervention in patients having diaphragmatic hernias.

There are two types of diaphragmatic hernia: the hiatus hernia and the true diaphragmatic hernia. Hiatus hernias can be subdivided into three types: hernia due to congenitally short esophagus, the paraesophageal hiatus hernia, and the esophagogastric hernia. In true diaphragmatic hernia, which is much less common, there is a weakness in the diaphragm, either traumatic or congenital in origin, through which the abdominal viscera can herniate. The etiology of the diaphragmatic hernia includes many factors. The acquired factor of greatest importance is, of course, trauma, which may be direct (that is, a laceration or penetrating wound of the diaphragm, with resultant herniation of the abdominal viscera), or indirect, (that is, occurring after a crushing-type injury or an inflammatory process).

Causes of the common type of hiatus hernia seem to include conditions producing increased abdominal pressure, such as pregnancy, obesity, ascites, straining, the wearing of tight garments, or tumor. Occasionally important in the etiology of diaphragmatic hernia are atrophy of the elastic tissues of the diaphragm, cicatricial shortening of the esophagus, and scleroderma.

REPORT OF CASES

CASE 1.—When a 42-year-old man was treated after a serious automobile accident, his chest appeared normal on roentgenograms. A few months later, he began to notice chest pain and marked shortness of breath when he exerted himself. X-ray films showed the large hiatus hernia. His stomach and part of the colon had herniated up through the diaphragm into his chest. His symptoms were due partly to the digestive upset resulting from the organs being in the chest, and partly to the dyspnea from the great displacement of the pulmonary capacity.

CASE 2.—A moderately obese woman complained of abdominal distress that was worse when she was lying down but was relieved when she got up. The x-ray films showed a large hiatus hernia with a tumor mass pressing on the lower portion of the stomach. We felt that the tumor, plus the increased intra-abdominal pressure, contributed to causation of the hiatus hernia. At surgery, we repaired the hiatus hernia and removed a large pancreatic cyst. The patient has been asymptomatic since the surgery, even though she has not lost weight.

CLINICAL FINDINGS

Congenital diaphragmatic hernia almost invariably causes symptoms shortly after birth. Physicians must recognize these symptoms early. If the defect is not corrected early, the child will die from cardiorespiratory failure or the secondary effects of intestinal obstruction. Occasionally persons with congenital hernia survive—sometimes to adulthood. Even then, the lesion will eventually produce symptoms at some stage, if not soon after birth.

Esophageal hiatus hernia, by far the commonest type of diaphragmatic hernia of clinical significance, may occur at any age. This lesion seldom produces symptoms before adult life.

SYMPTOMATOLOGY

The symptomatology of diaphragmatic hernia, especially of hiatus hernia, depends on many factors, most of which interfere either directly or indirectly with the motor function of the distal portion of the esophagus and of the thoracic viscera. Factors important in producing symptoms include the size of the hernia, the organs in-

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volved in the herniation, the inflammatory component in or around the esophageal lumen, and the degree of reflux esophagitis, as well as the thickness and consistency of the hiatal orifice.

The classical symptom is discomfort in the upper abdomen, which is most marked when the patient lies down and which is relieved when he stands up. The usual pain is confined to the epigastrium. Its severity is variable. At times the pain is substernal and may radiate to the left arm, much like the pain associated with coronary insufficiency. To add further to the confusion, the diphragmatic hernia may occasionally act as a trigger mechanism to produce anginal pain in patients with coronary artery disease. Retrosternal burning and a "sour stomach" are very common complaints. Dysphagia is the second most important symptom. It usually indicates some esophageal distortion or narrowing. This symptom suggests early obstructive phenomena, such as is illustrated in the following case history.

CASE 3.—Dysphagia developed in an 85-year-old woman during the year before surgery. At first, she was unable to swallow only solid foods; then she could not swallow soft foods; finally she could not even swallow liquid foods. Her dysphagia was accompanied by retrosternal pain that was suggestive of cardiac disease. She lost much weight over a two year period. Esophagoscopy revealed only an inflammatory reaction and stiffness of the lower end of the esophagus, but carcinoma could not be eliminated from the diagnosis. The patient was markedly anemic, although there had been no massive hemorrhage, and she had signs of nutritional deficiency. The roentgenograms showed marked obstruction because of the hiatus hernia. She did well following surgical repair of the lesion.

Besides the complaints already mentioned, there may be any degree of respiratory or gastrointestinal complaints, depending on the organs involved in the herniation. When a large volume of the stomach or intestines is herniated, there may be cyanosis. Postcordial distress is seen frequently when a considerable amount of the stomach has herniated into the chest. If the intestines are involved, there may be various manifestations of intestinal obstruction. On occasion, a complete intestinal obstruction may be the initial manifestation of diaphragmatic hernia. The significant feature of respiratory embarrassment is that it is invariably increased after eating and is severer after eating than after exertion.

CASE 4.—A 76-year-old man complained of pain in the upper abdomen, but his most marked symptom was dyspnea with cyanosis shortly after eating. This condition was frequently relieved with belching, and he had a tremendous amount of belching and regurgitation following meals. He had had a massive hemorrhage four years before, but no bleeding since then. After he had operative repair of a hiatus hernia, his symptoms were relieved. In the summer of 1952, he had a recurrent massive gastrointestinal hemorrhage from a duodenal ulcer, which was treated by subtotal gastrectomy.

Frequently associated with diaphragmatic hernia are such secondary changes as inhibition of growth in children on a nutritional basis, weight loss in adults because of the patient's fear of eating, and many of the symptoms relating to anemia, such as are present with bleeding from a hiatus hernia. Physicians should give more emphasis to these secondary changes, since many patients show serious changes that are indirect effects of the primary lesion.

Physical findings are variable and depend on the size of the hernia. As a rule, the physical signs are of little significance, but in extreme cases, if enough of the abdominal viscera are in the chest, very characteristic findings may be elicited on examination.

DIFFERENTIAL DIAGNOSIS

Diaphragmatic hernias are the greatest masqueraders of all abdominal conditions. In a large series of cases, we found that there were usually three incorrect impressions before we made a correct diagnosis. Conditions most commonly confused with diaphragmatic hernias are gallbladder disease, ulcer, carcinoma of the esophagus, and cardiac disease. The physician most commonly makes the correct diagnosis if he is aware of the possibility of hiatal hernia and looks for the symptoms of it. Roentgen examination or esophagoscopy confirms his clinical opinion. Esophagoscopy may reveal evidence of late reflux esophagitis or peptic ulcer. Almost invariably the esophagoscope will pass into the cardia of the stomach without encountering any resistance. It is difficult at times to make the differential diagnosis between carcinoma of the esophagus and esophageal hiatus hernia; considerable difficulty is encountered when the two conditions occur concomitantly. Gallbladder disease in association with diaphragmatic hernia is not an unusual finding; the physician may exercise considerable judgment in ascertaining which of the two conditions is responsible for the patient's symptoms. It is very embarrassing to get no relief of the symptoms after operating on a patient and then to find later that the complaints were due to some other disorder.

Recently, a patient gave a history of having had essentially no symptoms until he suddenly began to vomit blood and to have tarry stools. Fourteen transfusions were necessary to bring him out of shock. A gastrointestinal x-ray examination showed a massive hiatus hernia and a gastric ulcer. An abdominal approach was used at surgery. The lesion appeared to the surgeon and the pathologist to be grossly malignant at this time, so a total gastrectomy was done; three days later when the pathology report on tissues was returned, it showed a benign gastric ulcer with marked inflammatory reaction around it. If the ulcer had not been visualized, the surgeon might have repaired this lesion via the thorax.

TREATMENT

In our experience, all diaphragmatic hernias, especially hiatal hernias, are medical problems until proved otherwise. Medical treatment is very helpful in evaluating the severity of the symptoms. The most important phase of medical therapy is weight reduction, as many patients are obese and even a slight reduction of intra-abdominal pressure will relieve all complaints.

CASE 5.—A 45-year-old obese man complained of upper abdominal distress, belching, and heartburn; he felt some discomfort when lying down but felt relieved on getting up. The patient was put on a reducing regimen with small feedings; since his weight was reduced his symptoms have virtually disappeared.

Antispasmodics are valuable, but one should remember that occasionally the stronger antispasmodics may increase the symptoms. The patient should be instructed to avoid strenous exercise, particularly lifting. Associated factors, such as abdominal tumors, should be corrected. Many patients are awakened by severe pain at about 4 or 5 a. m. These patients are instructed to elevate the head of the bed on blocks at least 6 in. (15 cm.) in height if possible. They should also be instructed to sleep on the left side when this relieves the complaints.

INDICATIONS FOR SURGERY

As previously mentioned, most diaphragmatic hernias are medical problems. Surgery is indicated only for complications, the commonest of which is bleeding, either massive or occult, with secondary anemia.

CASE 6.—An 82-year-old man had severe anemia, with a hemoglobin level of 6 gm. per 100 cc. There had been no recent tarry stools or massive hemorrhage. He had, besides the anemia, a history of chest pain, which was suggestive of coronary insufficiency. The hiatus hernia and ulcer that had been seen on roentgenograms were relieved surgically, and the patient had marked relief of the anemia and of the coronary insufficiency symptoms postoperatively.

The second most common and serious complication is obstruction, which usually occurs at the junction of the stomach and the esophagus, even though a good deal of the stomach may be in the thoracic cavity.

CASE 7.—A 65-year-old woman had symptoms of marked dysphagia, regurgitation, and weight loss. She had complete relief of her symptoms after surgical management, and is still living a very comfortable life.

The third indication for surgery is the presence of intractable symptoms. These symptoms are not necessarily related to the size of the hernia; occasionally, a large hernia produces intractable symptoms because of its size. On the other hand, some of the small hiatal hernias can produce pain that is not relieved with ordinary symptomatic therapy. These are usually hernias having a small rigid orifice.

CASE 8.—A 67-year-old woman presented very typical symptoms of hiatus hernia. She was very obese, and she would not lose weight. She was operated on because of the intractable symptoms. She was completely relieved even though she maintained her obesity following surgery. At surgery, the dominant finding was a very tight hiatal orifice, and the hernia was firmly implanted in the thoracic cavity.

If the indications for surgery are rigidly adhered to, one will obtain good results; however, when symptoms are not specifically significant, surgery will not usually be helpful and may even be harmful. It is too easy to overlook another lesion in favor of a hiatal hernia, and we feel that the patient should have symptoms or indications sufficiently severe to justify surgery. It is extremely important to carry out complete studies on patients with uncomplicated hiatal hernias because the true cause of the symptoms may lie elsewhere. Many patients with hiatal hernias have no symptoms.

The following history represents one of the cases in which unfavorable results were obtained.

CASE 9.—A 52-year-old woman complained of substernal pain that was severest when she was lying down. There was no anemia, weight loss, or obstruction. The patient was operated on, but the symptoms were not relieved. There was an early recurrence of the hiatal hernia with the intestinal contents being pushed back up into the thoracic cavity. This type of patient can be managed better on a medical regimen, and in this case it would have been much better had she not been operated on even though symptoms were persistent.

In a group of 38 patients who were operated on, the ages varied from 36 to 87. In this group, the results in five were considered unsatisfactory because of a lack of relief of symptoms. There were two deaths. Both were from pulmonary emboli. It is interesting to note that in both of these instances the approach was subdiaphragmatic, and other abnormalities were treated surgically in addition to the hiatal hernia.

SUMMARY

Diaphragmatic hernia, a very common finding, may frequently present symptoms. The most important symptoms include epigastric discomfort at night relieved in an upright position, dysphagia, which occurs in more advanced cases, and anemia in a high percentage of cases. Surgery should be reserved for patients who have serious symptoms associated with hiatal hernia and particularly for cases with severe complications. If the surgical indications are rigidly adhered to, good results will follow surgical treatment of properly selected diaphragmatic hernias.

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Contact Dermatitis From Ointments.—With the introduction of many new external medications in the past decade, therapeutic contact dermatitis has become a major problem in the practice of dermatology. A considerable percentage of dermatologic patients have this complication. Four widely used groups of drugs have a relatively high incidence of contact dermatitis. The commonest sensitizers belong to the group of drugs which relieve itching because they have a local anesthetic action when applied to the skin. Among these are benzocaine, surfacaine, nupercaine and others. The antihistamines used locally are a good second among cutaneous sensitizers. Thephorin, pyribenzamine, benadryl, histadyl and others show a rising tendency to produce contact dermatitis. The antibiotics, used locally, have a high index of sensitivity. Penicillin, streptomycin and others may cause dermatitis. The sulfa drugs, particularly sulfathiazole, caused many cases of contact dermatitis, but fortunately their sensitizing properties became so well known that they are no longer used externally to any degree.

The general pattern of the development of therapeutic contact dermatitis is almost always the same. The medication is used on the local lesion for a variable period of time, from days to months. In the beginning there may be great relief of the symptoms of the original disease. The first evidence of sensitization is usually development of a dermatitis where none was present before, as in anogenital pruritus, or the aggravation of the original dermatitis. Within a matter of days after this local aggravation occurs a dermatitis appears in a rather consistent fashion. The hands and forearms are usually involved early; then the face, especially the eyelids and ears and down to the V of the neck; then the legs and feet. In these areas there is usually an edematous, oozing, itching dermatitis. If the medication is stopped the widespread dermatitis is the first to disappear, with the most recently involved areas being the first to clear, and the originally treated areas being the last to improve.—R. Nomland, M.D., Therapeutic Contact Dermatitis, *The Journal of the Iowa State Medical Society*, April, 1953.

PRIMARY FIBROSARCOMA OF THE SKIN

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In 1924, primary fibrosarcoma of the skin was distinguished as an entity and separated from other tumors because of its characteristic clinical and histological manifestations by Darier and Ferrand.[1] It is best known as dermatofibrosarcoma protuberans. Binkley [2] found that this neoplasm was first presented by Sherwell to the New York Dermatological Society in 1890, and Costa [3] states that Taylor also reported a case later in 1890. Many names have been given by different authors [4] to this neoplasm of the skin. The terminology of some authors suggested a benign tumor, while that of others indicated a malignant tumor. Woringer [5] and Senear [4d] and his associates called this tumor benign, while Eller,[6] Binkley,[2] and others believed it to be more serious.

Over 200 cases have been recorded, including 38 cases that Pack [7] recently reported. Hoffman [4b] was of the opinion that general surgeons excised the tumor because of the clinical impression that the tumor was extremely malignant and that the pathological diagnosis of fibrosarcoma, which was usually rendered, greatly overemphasized the degree of malignancy. Binkley [2] stated that pathologists frequently mistake this tumor for either a neurofibroma or a neurogenic sarcoma or give the diagnosis of fibrosarcoma, not specifying the type. Michelson [8] reported three different pathological diagnoses of the same tumor. The differences in nomenclature and interpretation of the pathological changes partially account for the apparent rarity of reports in the literature of this tumor.

The commonest sites of this tumor are the abdomen and back, but it has been described on every part of the cutaneous surface except the palms and soles. Once the tumor has developed, it varies greatly in size and shape. An early lesion may take one of several forms. 1. It may be almond-sized. 2. It may grow to be as large as a cantaloup and may consist of several pedunculated parts. Some of these peduncles are connected to the main tumor by a narrow stalk; others are attached by a broad base. 3. It may be a firm, broad, intracutaneous plaque with a small mound-like elevation superimposed. These tumors develop in the cutis and subcutis as small, hard, infiltrating nodules that increase in size and number to form a firm sclerotic plaque. This plaque may extend deeply, may invade the underlying adipose tissue, and has been known to become adherent to underlying fascia. This infiltration acts as a foundation that the protuberant growths utilize for support. The color of the external surface of the tumor varies; it may be the color of normal skin, pink, or red, depending on the vascularity of that particular tumor. The surface at first is smooth, but, later, the elevated growths make their appearance and the epidermis covering the tumor becomes thinned and eroded and, finally, ulcerated. These tumors are generally hard, almost cartilaginous, but may become soft after erosion or ulceration. Early recurrence and rapid growth often follow incomplete removal. These tumors are usually painless. Hemorrhage may occur during the growth of the tumors, and, eventually, gangrene may result. The only satisfactory method of treatment is complete and wide excision. A considerable zone of normal tissue must be included in the excision to insure a permanent cure. Senear and his co-workers [4d] state that the lesion is practically asymptomatic and does not affect the general health. Becker and Obermayer [9] stated that the rare condition of dermatofibrosarcoma is practically asymptomatic and does not affect the general health of the patient nor does the tumor metastasize. Binkley, however, reported several instances in which metastases occurred and cited a case in which the tumor was first noted in 1890; it was excised but recurred five times at the same site. His patient died of tumor metastases in 1928. Hertzler [4a] described fibrosarcomatous tumors of the skin and stated that these tumors could not be rare as, in 25 years, he found 22 out of 5,000 tumors to be this type. He further stated that complete excision of the tumor results in a permanent cure, that, if recurrence follows inadequate removal, a wide, second excision may still result in a cure, and that, even in cases in which there is regional metastasis, the involved lymph nodes may be removed successfully. Hertzler also reported that, in an instance in which seven operations had been performed for such a neoplasm, the patient was well some 20 years later. Internal metastases have also been reported by other authors.[10] Patients have been recorded in whom this condition lasted as long as 50 years. Several such tumors have occurred in old surgical scars, but these may have been local recurrences.

Lymph node and pulmonary metastases constitute the chief causes of the fatal termination of fibrosarcomas. A most important clinical procedure is the routine roentgenographic examination of the chest in every patient suspected of having malignant disease, including fibrosarcoma of the skin. Saltzman,[11] in discussing the prognosis of fibrosarcoma, stated that the prognosis is more favorable when the tumor arises from the skin. He arrived at this conclusion from a study of 80 patients treated between 1936 and 1948.

Lamb, in discussing Binkley's paper, stated that, in dealing with a malignant tumor of this type, excision should be preceded by heavy doses of roentgen irradiation and that wide dissection should be followed by further irradiation. A fibrosarcoma, however, is a highly radioresistant tumor,[12] and I feel that irradiation therapy is contraindicated. Wide excision is a more definitive procedure and insures a cure, provided metastasis has not already occurred. Furthermore, the malignant potentiality of this tumor is extremely low, and, even in known cases of metastases, the life expectancy is quite long. To risk the possibility of a radiodermatitis as a consequence of the large roentgen doses needed for treatment of fibrosarcomas seems unwarranted. Irradiation may result in the ultimate development of squamous cell carcinoma on the damaged skin, which is a much more malignant neoplasm than the original fibrosarcoma.

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Because of space limitations, all of the bibliographic footnotes have been omitted from THE JOURNAL and will appear in the author's reprints.

Pathological Diagnosis.—Mopper and Pinkus [13] feel that the diagnosis of fibrosarcoma is frequently suggested by the history and physical examination and that histological studies are confirmatory. They were in agreement with Ormsby and Montgomery's [14] statement that differentiation lies midway between the ordinary fibrosarcoma and the dermatofibroma lenticulare, although individual microscopic fields could be selected that resemble one or the other. Examination of several sections of the tumor, however, will reveal the characteristic picture. Basically, the composition is that of a low grade fibrosarcoma, but there may be large lacunas and myxomatous changes.

Cause.—The cause of fibrosarcoma is unknown. While trauma has been associated with a number of cases, its incidence is relatively low and may have been only coincidental. Binkley [2] theorized that, because of the unusual predilection of these tumors to be located near the right or left of the midline, there was possibly a relationship to the embryologic mammary ridge. Many tumors have been recorded that do not conform to this concept, since their location had no relation to the mammary ridge. The possibility of misplaced embryologic mammary ridge tissue must not be overlooked, but in very few cases has the location of this tumor had any relationship to mammary tissue. Also, the absence of epithelial elements in these tumors is a significant argument against this theory.

Degree of Malignancy.—This tumor must be considered to be a malignant growth, both locally and systemically. The criteria for malignancy include invasion and metastasis or both, and this tumor satisfies these conditions. Its malignant potentialities are much less than those of a fascial fibrosarcoma, and the long duration of many of these tumors attests to their relatively low malignant potentialities. Several deaths have been proved to be the result of metastases, particularly pulmonary, from fibrosarcoma. Tumors that approach the fibroma in histological appearance are much more benign than the more cellular lesions at the opposite end of the spectrum, namely a spindle cell sarcoma. Regardless of the relative benignity of the individual tumor, if it is not a fibroma, it must be considered to be malignant.

REPORT OF CASES

CASE 1.[15]—A white man, 41 years of age, had noticed a small area of numbness on his back 20 to 25 years before admission to the hospital. About 10 years before admission, three small nodules developed in the medial border of the lesion. These slowly enlarged and coalesced to form the tumor mass present on admission. Examination showed a firm, brownish-red, intracutaneous plaque in the region of the left scapula. The lesion measured 7 by 9 cm., was slightly elevated, and showed, at the medial border, a group of nodules that measured from 1 to 1.5 cm. in thickness. Histological studies indicated that this tumor stood at the benign end of the spectrum that this peculiar group of dermatofibrosarcoma presents; highly cellular lesions, indistinguishable from spindle cell sarcoma, are at the other end.

CASE 2.[16]—A 49-year-old, obese Negro woman had a nodular tumor on the anteromedial aspect of the left thigh. The lesion was reddish, measured 5 by 3 by 4 cm., and was composed of several confluent protuberances. The skin covering the tumor was thin and shiny, with dilated blood vessels. The skin for a distance of 2 cm. around the base was infiltrated by a firm plaque that extended into the subcutaneous panniculus. The patient had first noticed a small area of redness in this region nine years before admission. This grew slowly at first and more rapidly in the year preceding admission. Bleeding was serious enough to cause the patient to seek medical assistance. A biopsy and microscopic examination led to the diagnosis of fibrosarcoma of the skin. The tumor was excised widely.

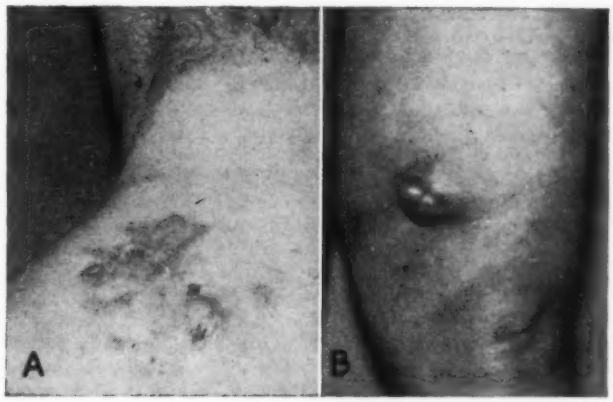

Fig. 1.—*A*, the tumor in case 1. There were no protuberances, and the lesion was primarily an intracutaneous plaque. *B*, the tumor in case 2. This was an early protuberant lesion.

CASE 3.[17]—The history of this patient was presented to the Detroit Dermatological Society, March 15, 1927. This 38-year-old man had noted a small mass on the left side of the forehead some 10 years before. It slowly enlarged, and it was incised and a serous fluid was drained from it. Other masses appeared on the forehead, and these too enlarged. They recurred after excision on two separate occasions. On March 15, 1927, there were firm, nodular masses surrounding the scar left by the excisions and an erythematous tumor at the border of the scalp. The surface of the nodules was telangiectatic. The pathologist reported the tumor to be a nonencapsulated cellular fibroma, suggestive of fibrosarcoma. The photograph of this patient (fig. 3) was taken some time after he was presented to the society. The clinical aspects of this case are very similar to those in a case reported by Costa.[3]

CASE 4.—A Negro man, 67 years of age, was admitted to Detroit Receiving Hospital on Dec. 12, 1946. He stated that he was in perfect health until nine months before, when a small tumor developed on the right upper arm. It progressively enlarged. Examination revealed a large, fungating growth about 2.5 in. (3.8 cm.) in diameter and approximately the shape of an orange. It was located on the lateral aspect of the

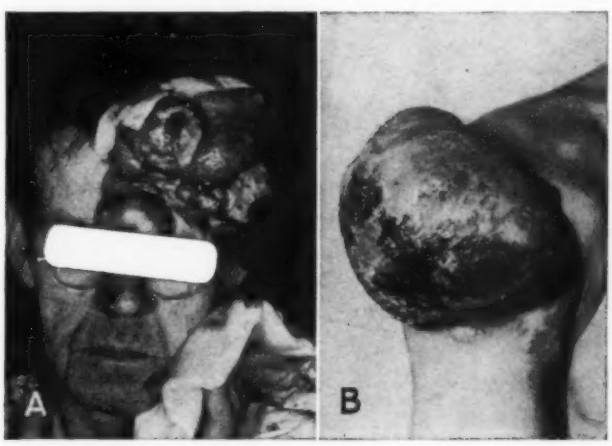

Fig. 2.—*A*, the tumor in case 3, which is an unusual demonstration of the protuberances that sometimes occur in this disease. *B*, the cantaloup-sized tumor on the right upper arm of patient in case 4. Note lymph node enlargement from metastases.

right upper arm near the shoulder joint. This fungating mass was a bright reddish-purple color and was attached to the skin on a broad base. This tumor was excised on Dec. 17, 1946, and there was some gangrenous tissue below the tumor that extended down to the deltoid muscle but did not involve it. The diagnosis rendered after pathological examination was myxofibrosarcoma.

This patient was admitted to the Wayne County General Hospital in December, 1947. Examination at that time revealed a large lobulated mass on the right shoulder girdle. The skin surface was ulcerated. The mass measured 13.5 by 11.5 by 11 cm. It was attached by a constricted, broad pedicle measuring 9 cm. in diameter. Several large axillary nodes were palpated. The right arm was amputated above the tumor. After study of the tissue, the diagnosis of metastatic, highly malignant myxofibrosarcoma was made. A roentgenogram of the chest made on Oct. 20, 1947, showed no evidence of pulmonary metastases. There was no bony involvement.

The patient was readmitted on May 4, 1948, to the Wayne County General Hospital. At that time there were several nodules at the site of the amputation. A roentgenogram of the chest made on May 4, 1948, showed multiple metastases. The patient died of uremia on May 30, 1948. Slides of the tumor sections that were made in December, 1946, were reexamined recently and interpreted as being, in some fields, an example of primary fibrosarcoma of the skin. Other microscopic fields showed more edema, while others showed inflammatory foci secondary to ulceration and infection. Several areas showed a liberal sprinkling of multinucleated cells, but this did not change the diagnosis. The protuberances of the lesions were certainly quite visible in these sections.

CASE 5.—This man had had a growing mass at the base of the left side of the neck for the seven or eight months preceding admission. It had grown quite rapidly in the last two months before admission. The tumor was in an area from

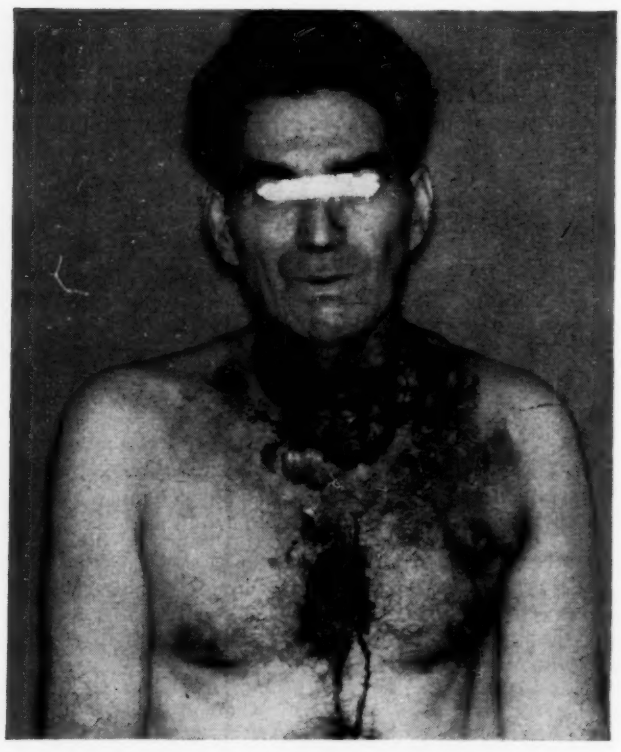

Fig. 3.—Patient in case 5. Note intracutaneous metastatic lesion.

which a similar growth had been removed some 37 years previously in Greece. The patient at that time was 15 years old. His general health had otherwise been good. Physical examination revealed, at the base of the left side of his neck, anteriorly, a firm mass that was larger than a fist. No pulsation was felt. Roentgenographic studies showed a soft tissue mass, no bone destruction, and a normal chest.

The tumor was excised on Feb. 12, 1948, and the skin was found to be involved with several tumor nodules. The pathologist reported that this tumor was a spindle cell sarcoma, probably of neurogenic origin, and that it was apt to recur locally but not apt to form metastases. Postoperatively, the patient was given 36 deep x-ray treatments. He was readmitted to the same hospital on Aug. 11, 1949, with a large fungating mass

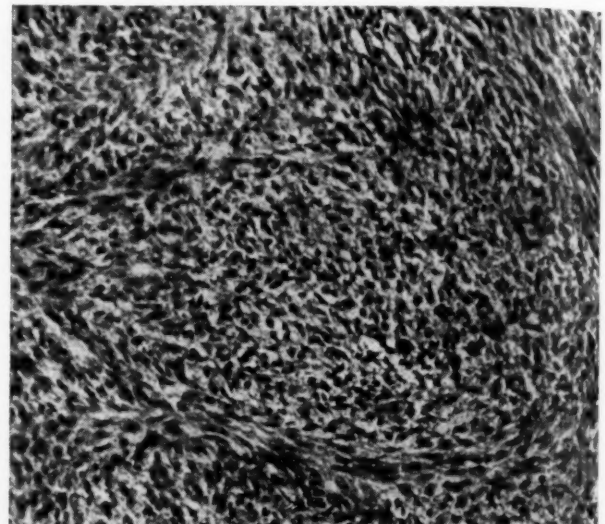

Fig. 4.—High power magnification of a cellular section of primary sarcoma of the skin.

on the left side of the neck and chest that had recurred just eight months previously. There was moderate ulceration and bleeding. A biopsy indicated a myxofibrosarcoma. On Oct. 10, 1949, prior to surgery, the patient was given thiopental (Pentothal) sodium at 12:15 p. m. He was pronounced dead at 12:17 p. m. Slides of tumor sections were recently reexamined, and interpreted as being compatible with primary fibrosarcoma of the skin. Areas were present that were quite fibrotic, while others showed a marked myxomatous change. Several fields revealed characteristic fibrosarcoma of the skin.

SUMMARY AND CONCLUSIONS

The term primary fibrosarcoma of the skin is preferred to dermatofibrosarcoma protuberans or other previous designations because of its simplicity. This term is also adequate to cover the cases in which protuberant growths are not present. The prognosis of dermatofibrosarcoma protuberans is much better than that of other fibrosarcomas, since its metastatic tendencies are slight and long delayed. It must, however, be considered a malignant tumor.

Fibrosarcoma of the skin has a strong tendency to form large protuberant masses, and wide surgical excision is the treatment of choice. Roentgen or radium therapy should not be employed, as the large doses required may produce a radiodermatitis with possible development of a more serious malignant growth.

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ALOPECIA LEPROTICA: ITS RELATIONSHIP TO TRANSMISSION OF LEPROSY

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There is ample evidence that there are distinct clinical variations of leprosy in different world areas.[1] The role of host susceptibility or resistance, racial factors, and climatic and other geographical conditions in producing these variations remains an unsettled problem.[2] In this paper a correlation will be made between one variant, alopecia leprotica, and the religious customs and folklore of the countries influenced by Buddhism. Fortunately, a natural experiment on babies is found in certain regions of the world where Buddhism is practiced, allowing the leprologist to use babies as a comparative test group of the contagiousness of leprosy, with the babies in the remainder of the world as controls. The basis of the experiment rests in the widespread custom among the Buddhists of shaving the heads of the newborn. Evidence will be presented to show that leprosy is contracted during infancy or childhood and not primarily in maturity.

CULTURAL BACKGROUND

Buddhist priests migrated from China through Korea to Japan approximately 1,300 or 1,400 years ago. With this migration the custom of clipping the scalp of newborn infants was introduced into the latter areas. When the razor became readily available for general use about 200 years ago, the habit of clipping was replaced by shaving the heads. This ritual was performed on the newborn on certain days, namely, at 7 days of age when the infant's umbilicus was believed to be drying up satisfactorily, at 30 days when it was felt that the baby would survive, and at 90 days when solid or semisolid foods were first given. Both boy and girl babies were shaved, the girls until they were 4 years of age and the boys until they were 8 or 9 years of age. In a few instances the custom was practiced on boys to the age of 12.[3]

The predominant religion in Japan is Buddhism, which is divided into five different sects. The shaving custom is still observed in certain prefectures, especially in the rural areas and among the older age groups. The younger generation, particularly in Tokyo, is not well acquainted with this ritual. Christianity, as yet, has had little influence on this custom in regions where it is extant.[3]

The religious culture in Korea is derived from China, with two predominant religions, Buddhism and Confucianism. Among the followers of each the habit of shaving the head of the newborn is conventional. There is, in addition, a small Christian group. The Formosans migrated primarily from Fukien Province, China. They forced the original native group into the hills and mountainous regions of the island. As a consequence, the predominant religions are Confucianism and Buddhism and the practice of shaving the scalp of infants is universally observed. In China the custom of shaving the head of the newborn is an accepted universal procedure and is performed at 30 and 90 days.[4]

METHODS AND MATERIAL

Leprosariums in Japan, Korea, and Formosa were visited to determine whether the incidence of alopecia leprotica was greater in relation to the total number of patients in the leprosariums of these countries than in other countries where the practice of shaving the scalp of newborns is not observed. Careful examination in each case was performed to rule out baldness from other causes, particularly the typical type of male baldness (alopecia senilis). Characteristically, lepromatous alopecia could be grouped into three types. The first was an almost complete baldness, with only a few patches of hair remaining (fig. 1). The second type presented a moth-eaten appearance with scattered involvement of the total scalp (fig. 2). The third group showed a patchy involvement, varying in size with intervening areas appearing grossly normal (fig. 3). The latter type was more difficult to recognize, especially in long-haired females where the involved areas could be easily hidden.

TABLE 1.—*Incidence of Leprotic Alopecia in Inmates of Leprosariums in Some Asiatic Areas*

Place		No. of Lepers	No. with Leprotic Alopecia	Percentage
Japan	Male	378	186	49.18
	Female	211	82	38.86
	Total	589	268	45.50
Korea	Male	264	72	25.75
	Female	259	82	31.66
	Total	523	154	29.44
Taiwan (Formosa)	Male	137	35	25.55
	Female	71	11	15.49
	Total	208	46	22.11
Chinese soldiers	Male	38	11	28.95
Total	Male	817	304	37.20
	Female	541	175	32.34
	Total	1,358	479	35.27

RESULTS

The total Japanese population in the leprosarium situated at Tama Tenshoen, near Tokyo, Japan, was 1,100, of which 700 were males and 400 females. In this institution 589 lepers were examined, including 378 males and 211 females. Of these, 186 of the men and 82 of the women showed typical scalp involvement suggestive of lepromatous origin (table 1).

Two leprosariums were visited in Korea, one in the vicinity of Taegu and the other near Pusan. Of the total

From the Letterman Army Hospital.

Owing to lack of space, some of the bibliographic references have been omitted from THE JOURNAL and will appear only in the authors' reprints.

3. Yanagida, K., Professor of Anthropology, Tokyo University, Tokyo: Personal communication to the authors.

4. General Chen Li-Kai, Surgeon General, Chinese Army, Taipeh, (Formosa) Taiwan: Personal communication to the authors.

population of approximately 1,500, 523 were examined; 264 of these were male and 259 were female. Seventy-two men and 82 women showed definite lepromatous alopecia (table 1).

Formosa has one leprosarium at Taipeh. Of the 480 inmates, 55 were Chinese soldiers from the Chinese

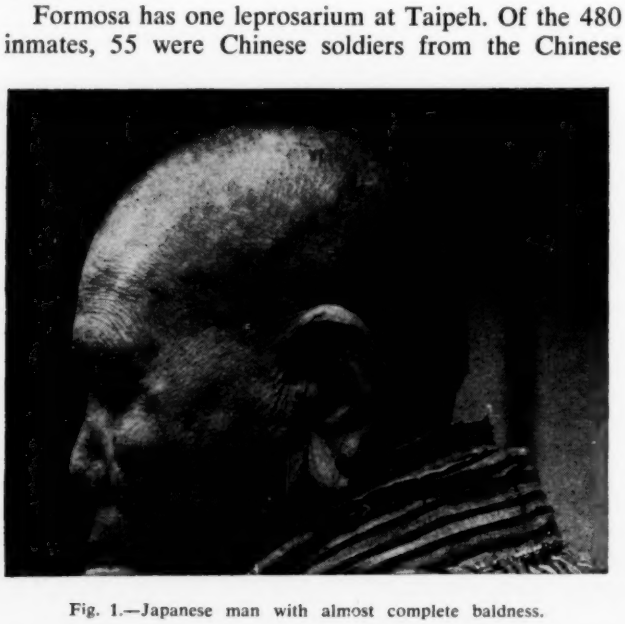

Fig. 1.—Japanese man with almost complete baldness.

Nationalist Army. At this institution 208 lepers, 137 male and 71 female, were minutely examined. Thirty-five men and 11 women showed lepromatous alopecia. Of the 49 Chinese soldiers examined, 11 were found to have scalp involvement of leprosy (table 1).

Histological verification of the clinical diagnosis was obtained by scalp biopsy in 20 cases selected at random in the Tama Tenshoen Leprosarium. The microscopic picture was similar in all cases, showing marked lympho-

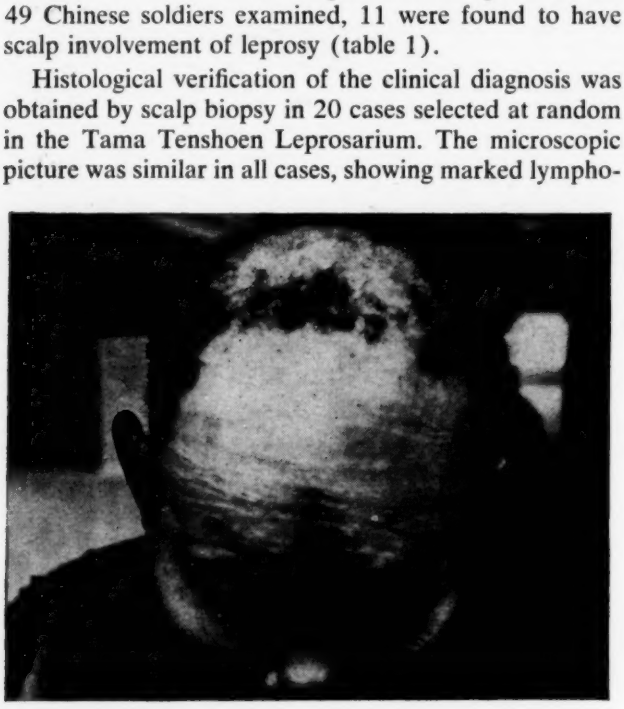

Fig. 2.—Japanese man with baldness with a moth-eaten appearance.

cytic infiltration, persistent involvement of the sweat glands, and the presence of varying numbers of macrophages. In 15 of the sections the acid-fast bacillus was easily demonstrated (fig. 4 and 5). In all sections the lesions were considered lepromatous.

In the final count of 1,369 persons with leprosy examined in three countries (Japan, Korea, and Formosa) where shaving of the newborn's scalp is practiced, 479 patients (35%) were found to have alopecia leprotica. The incidence in the male was only slightly greater than in the female (37% to 32%). The highest incidence, 49% and 38%, was found in the Japanese males and females, respectively (table 1).

Statistics from 11 countries where the custom of shaving the heads of infants is not present (Mexico, Venezuela, Philippine Islands, Sumatra, Egypt, Palestine, Norway, South Africa, Argentina, United States, and Hawaii) have been used in establishing the control group. Of 12,585 patients examined, only 34 were found to have alopecia leprotica. This is an incidence of less than 0.3% [5] (table 2).

In the Philippine Islands there have been no reported cases of alopecia leprotica. In order to contrast the histological sections obtained from patients with this abnor-

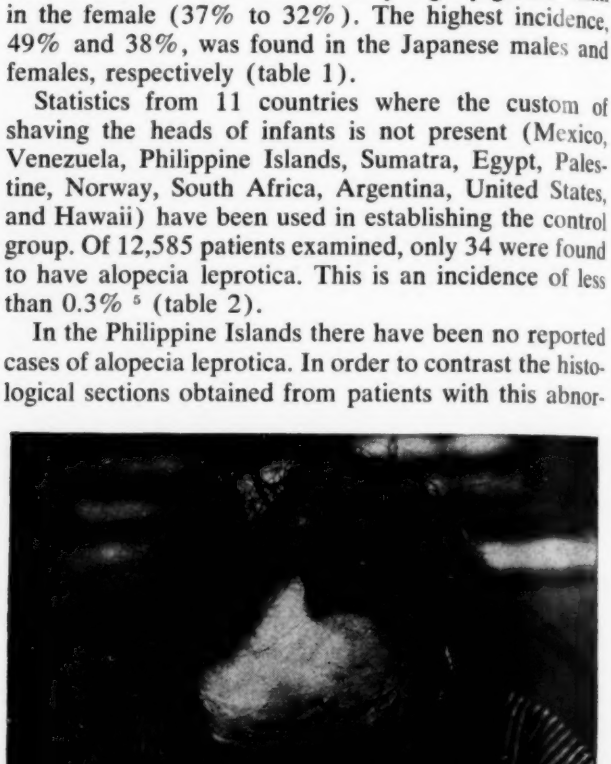

Fig. 3.—Japanese woman with the patchy type of baldness.

mality, biopsy specimens from the Tama Tenshoen patients were compared with scalp biopsy specimens taken by Manalang from 48 Filipino patients.[6] In each instance of the latter the microlepromatous lesions extended from the hairline upward, with normal tissue present near the vertex of the scalp. The sections from the Japanese scalps showed a macrolepromatous lesion.

COMMENT

It appears evident from the data presented that the incidence of alopecia leprotica among patients with leprosy is far greater in those countries where shaving of the scalp of the newborn is a common practice than where it is not. In this regard, the striking difference between the microscopic findings in scalp biopsy specimens taken from Japanese with lepromatous alopecia and from Filipinos without this clinical manifestation is of interest.[6] Large infiltrations of the face and ears, with subsequent loss of eyebrow hair, occur in all races and are a usual occurrence in the disease. The scalp invasion among the natives of Japan, Korea, and Formosa might theoretically

5. Hayashi, F.: The Anti-leprosy Works in Various Parts of the World as I Have Seen Them, J. Pub. Health A., Japan **10**: 1-13 (Sept.) 1934. Manalang, C.: The Transmission of Leprosy, Havana, Cuba, Memoria Fifth International Leprosy Congress, 1948, p. 758.

be due to a greater virulence of the organisms, lesser resistance of the scalp, or greater dosage of the organism. These possibilities appear unlikely when one considers the heterogeneity of the test groups and the geographical separation of these groups. The common factor in all cases appears to be the larger dosage of the organism, for trauma (including shaving) with complete removal of the natural protecting barrier of the hair and the inevitable production of small nicks and cuts would appear to predispose to heavy infection.[7] It is clear that scalp infection is external in origin and not vascular from a central focus.

In numerous infectious diseases the etiological agents characteristically escape from the host through the secretions or excretions of the affected organs or glands to infect new victims. In leprosy the pathological involvement of the sudoriferous glands and nerves is well established [8]; consequently, the infectious agent must at some time leave the host through the medium of sweat gland secretions. It seems likely that leprosy is spread in infancy by prolonged and frequent skin-to-skin contact between the child and the person with leprosy. The distribution of initial skin lesions in children at the Culion Leper Colony, Philippine Islands, was found to correspond very closely to those exposed parts of the body that were brought into direct pressure contact when the child was carried during infancy. As a rule, the mother, or occasionally another member of the family, is accustomed to carry the child in her bare arms with her hands, holding it by its buttocks or upper thighs. The most frequent sites of skin lesions found in these children were on both cheeks of the face, the lower posterolateral area of the arms, elbows, and upper medial area of the forearms, the external parts of both buttocks, the upper anterolateral thighs, both knees, and the anterior parts of the upper legs.[9] With some variation, these areas coincide fairly well with the most frequently involved areas in adults with leprosy.

TABLE 2.—*Incidence of Leprotic Alopecia in Patients with Leprosy in Various Countries*

Places	Leprosarium	No. of Lepers	No. with Leprotic Alopecia
Mexico, Asilam	Pedro Lopez	38	..
Venezuela (Caracas)	.....	1,656	..
Philippines	.....	6,000	0
Sumatra	Pelantoengan	167	10 (5 Chinese & Malayan, 5 European & Eurasian)
	Suerabaya	154	1 (Native)
	Sungai Buloh	1,200	1 (Chinese)
Sumatra	Hoeta Salem	500	1
	Laoe Si Momo	400	1
	Belawan Deli	450	4 (3 Chinese, 1 Javanese)
Egypt	.....	..	0
Palestine	Jerusalem	25	1
Norway	Bergen	88	0
South Africa	Pretoria	975	6 (5 Native, 1 Cape Negro)
Argentina	Muniz	182	3
United States	Carville	350	5 (2 white, 3 mixed blood)
Hawaii	Kalaupapa, Molokai	459	1 (Japanese)
	Total.....	12,585	34

The natural history of the transmission of leprosy was given considerable elucidation by the important works of Brazil investigators [10] and Lara.[9] The former found that the disease developed in over 70% of the children affected prior to the third year. In Culion, Philippine Islands, Lara repeatedly examined 770 children over a period of years in an effort to determine the pathogenesis of leprosy in these cases. The children ranged in age from 1 to 9 years. Lara estimated that at least 50% of exposed children of leprous persons would show manifestations of the disease by the time they were 5 years old. He felt that the rate was identical for both sexes. This is in marked contrast to the 600 children of nonleprous employees of Culion Colony. During the past 25 years not a single case of leprosy has been found in these children despite yearly examinations. The employees and their families live in close proximity to the colony proper.

Fig. 4.—Biopsy specimen of scalp under low power magnification showing atrophy of hair follicles and lepromatous infiltration.

Similar evidence that direct contact is necessary for leprosy to be transmitted to children has been found in many parts of the world. In Punjab, India,[11] children of leprous parents are reared separately from their parents. In 30 years only one case of leprosy has developed among these children. Brazil has, for over 20 years, separated infants at birth from the leprous parent.[12] No cases of leprosy have developed among these infants.[13] In the Kalaupapa Leper Settlement, Hawaii,[14] the infant was likewise separated from the leprous parent as soon as it was born. The children were placed in a nursery within

9. Lara, C. B.: Leprosy in Infancy and Childhood, Monthly Bull. Bureau of Health, Manila, P. I. **24**: 61-89 (March-April) 1948.

12. Souza Campos, N.: Personal communication to the authors.

14. Hasseltine, H. E.: The Results of the Removal of Children Born of Leprous Parents to Clean Environment and Their Maintenance Therein, U. S. Pub. Health Bull. **141**: 55-72 (July) 1924.

the colony proper and were attended by supposedly healthy Hawaiians (largely relatives of the inmates). The latter were allowed to mingle freely with the inmates as companions and helpers. Later some of the children were released to relatives and others who were supposedly nonleprous. Of 219 children who were thus studied, leprosy subsequently developed in 10.[15] Possible leprosy was reported in 25 others. It is believed that the nature of care given these children did not exclude recurrent contact with persons with unapparent leprosy.

Human beings afflicted with leprosy, particularly when in the active lepromatous form, are generally recognized as the principal, if not the only, source of infection.[16] An interesting survey of the entire population of two communities in the Philippine Islands was made by Rodriguez and others.[17] They found that the incidence of

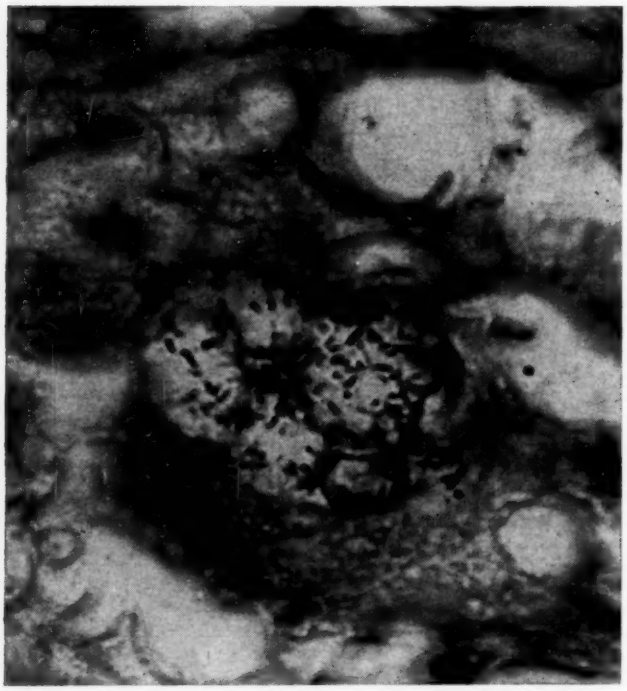

Fig. 5.—Specimen under high power magnification showing a typical lepra cell with lepra bacillus.

infection in persons exposed to cases of leprosy in the household was four times the rate in the whole community. One of these communities had a high leprosy incidence rate, the other city a low rate.[18] A Japanese study [19] of 21 villages near Sendai showed a leprosy rate of approximately twice the expected rate. It was found that all 66 patients lived in 44 houses among 53 blood relatives. The other 1,707 houses were free of leprosy. Numerous other observers [20] have found that leprosy is not regularly distributed in any infected area, but tends to occur in groups in certain villages, whereas nearby settlements may escape the disease entirely. In most instances there is an increased family occurrence, whereas some leprous persons with no family history of leprosy may have a relative admitted with the disease afterward.[21]

Environmental factors are felt to influence the transmission of leprosy. Such variants as a hot, humid climate, overcrowding, poor housing, and insufficient food and clothing have been implicated. Nevertheless, studies conducted in areas in both the Philippine Islands [22] and India [23] have failed to support this contention. Regions that were adjacent to each other and that resembled each other in most respects, including climate, housing, diet, poverty and filth, were found to have markedly different prevalence of the disease. A significant number of cases of leprosy have been found among the well-to-do native and European families in Dutch Guiana,[24] which would appear to vitiate poor environmental factors as contributing factors.

Evidence to support the contention that leprosy may develop in previously healthy adults does not appear to be nearly as conclusive as that referable to susceptibility in children. The incidence of development of leprosy among presumably healthy adults in close contact with the disease, such as attendants and relatives at various leprosariums, is similar to, but not greater than, the incidence of epidemic foci in the general population. There has never been an instance of transmission of leprosy to any attendant at the Saint Louis Hospital (Paris),[25] the Palesco Leprosy Colony (Panama),[26] or the National Leprosarium (Louisiana).[25] The rate of infection in husband or wife is similar to the leprosy rate for the country.[27] It would appear, thus, that conjugal or other intimate adult contact with a leprous person may have no epidemiological significance. Attempts to transmit leprosy from man to man by inoculation in 145 cases [28] failed in every instance but one. The patient in whom leprosy developed had a leprous son and other relatives with the disease and it is not certain, therefore, that the disease was absent at the onset of the experiment.[29] There are, in the literature, a few reports of inoculated infections in isolated instances.[30] Hasseltine and others reported a few cases, in which, on the basis of history alone, they felt the disease was contracted by adults.[31]

In view of the rather equivocal evidence as to primary adult infection with leprosy as compared to the much more abundant evidence supporting the development of childhood leprosy, the work of Cochrane [32] dealing with the tendency toward regression of leprosy and its self-healing nature in early infection is of interest. The recent report from Brazil [33] corroborates the previously reported findings of regression and in some instances progression of leprous lesions. About 65% of all children with the disease show healing or resolution of all recognized lesions without recurrence for from 1 to 13 years.[34] Almost all of them will show regression for as long as five years.[35] It may be postulated that a certain number of cases that are first recognized in adult life may very well represent the reappearance of a lesion that had lain dormant for many years.

18*b*. Guinto, R. S.; Doull, J. A.; Bancroft, H., and Rodriguez, J. N.: A Field Study of Leprosy in Cordova, Philippines: Resurvey in 1941 After Eight Years, Internat. J. Leprosy **19**: 117-135 (April-June) 1951.

21. Denney, O. E.: A Statistical Study of Leprosy in the Philippine Islands, J. A. M. A. **69**: 2171 (Dec. 29) 1917.

25. Strong, R. P.: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, ed. 6, Philadelphia, Blakiston Company, 1943, p. 826.

28. St. M. Mouritz, A. A.: Human Inoculation Experiments in Hawaii, Including Notes on Those of Arning and of Fitch, condensed by H. W. Wade, Internat. J. Leprosy **19**: 203-215 (April-June) 1951.

33. Souza Campos, N., and De Souza Lima, L.: Lepra Na Infancia, Rio de Janeiro, Brasil, Servico National de Lepra, 1950, p. 46-70.

SUMMARY

In leprosariums in Japan, Korea, and Formosa 1,369 patients with leprosy were examined for alopecia leprotica. In these countries the habit of shaving the scalp of newborn infants is a common practice. The lesion was found in 479 patients, an incidence of 35%. This is compared with an incidence of 0.3% reported in 11 countries where shaving the hair of infants is not customary. Evidence has been presented to show that leprosy is contracted by an infant through skin-to-skin contact with a leprous person. Contraction of leprosy by healthy adults is rare, and most reported cases are open to question. The data presented corroborate the findings of adult immunity and childhood susceptibility. The control of leprosy is effected by the separation of the leprous person from the infant or child.

TREATMENT OF MELANIN HYPERPIGMENTATION

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and
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Abnormal increases in melanin pigmentation of the skin have always presented a difficult problem to man because of their cosmetic and social significance. Disfiguring pigmentation of the exposed areas may have important and lasting effects on the emotional well-being of the patient. In addition, the quantity of melanin in the skin may determine the status of a person in a given society. To our knowledge little stimulus for the study of the mechanism of melanin formation has resulted from attempts to explain or modify the great variations in pigment seen in different races. Rather, the stimulus for investigation has come from observations on abnormal subjects including patients with Addison's disease, vitiligo, and hyperpigmentation of pregnancy, and from attempts to explain melanin production in plants, insects, and marine animals. As a result of these studies, much is known of the process by which the amino acid tyrosine

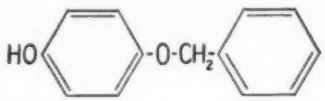

Fig. 1.—Monobenzyl ether of hydroquinone.

is catalytically oxidized by tyrosinase, a copper-containing enzyme, to melanin in the cytoplasm of melanocytes* of the skin, eyes, and leptomeninges.[1]

Attempts to treat areas of melanin hyperpigmentation have been manifold. Such agents as ammoniated mercury and hypochlorite bleaches have been used frequently but without success. About 14 years ago a group of Negro workers were noted to have depigmentation of the hands after wearing rubber gloves.[2] It was found that monobenzyl ether of hydroquinone (fig. 1), an antioxidant for rubber, was the active agent that produced the depigmentation. Since then, occasional reports have appeared on efforts to use crude monobenzyl ether of hydroquinone therapeutically to treat disorders of melanin hyperpigmentation. Although treatment was not very successful because of irregular results and sensitization reactions, some dermatologists continued using the drug in ointment form. In the past few years a purified and finely dispersed concentrated preparation of monobenzyl ether of hydroquinone (Benoquin) has become available for clinical study.† Following is a report of the results obtained by several dermatologists using this preparation in the treatment of 84 patients with melanin hyperpigmentation.

TERMINOLOGY

Before the presentation of clinical data, the terminology used to describe abnormal conditions of melanin hyperpigmentation will be considered. Only the commoner disorders will be discussed, as a detailed report will be presented elsewhere.[3] Throughout this report the term melasma will refer to hyperpigmentation occurring usually on the exposed areas, such as the face, neck, hands, and arms, associated in some instances with an increase in serum copper and urinary melanocyte stimulating hormone (MSH).[4] These changes may be related to increased pituitary gland activity. Among the conditions associated with disorders of hyperpigmentation designated as melasma are chloasma, Riehl's melanosis, Civatte's disease, Addison's disease, and chronic malnutrition. When a known underlying condition is associated with the melasma, such as pregnancy or Addison's disease, the terms melasma (pregnancy) or melasma (Addison) will be used. If no physiological disturbance is evident and there is simply hyperpigmentation of the exposed areas, only the single term melasma will be used.

The common term freckles rather than ephelides will be used to designate the ordinary small, flat, pigmented macules usually seen on areas exposed to sunlight. Microscopically these lesions show only increased pigment in the basal cell layer without increase in the number of melanocytes. A *café au lait* spot indicates an isolated pig-

Because of lack of space, some of the bibliographic references have been omitted from THE JOURNAL and will appear in the authors' reprints.

From the Department of Dermatology, University of Oregon Medical School. The work reported on in this paper was carried out by the authors during the past four years at the following institutions: Western Reserve Medical School, Cleveland; Mayo Foundation, Rochester, Minn.; University of Michigan Medical School, Ann Arbor, Mich.; and University of Oregon Medical School.

* In accordance with terminology adopted at the Pigment Cell Conference, New York, 1951, the term melanocyte will be used to designate the mature pigment-forming cell thus replacing the older term melanoblast.

1. Lerner, A. B., and Fitzpatrick, T. B.: Biochemistry of Melanin Formation, Physiol. Rev. **30**: 91, 1950.

2. Oliver, E. A.; Schwartz, L., and Warren, L. H.: Occupational Leukoderma: Preliminary Report, J. A.M. A. **113**: 927 (Sept. 2) 1939. Schwartz, L.; Oliver, E. A., and Warren, L. H.: Occupational Leukoderma, Pub. Health Rep. **55**: 1111, 1940.

† The monobenzyl ether of hydroquinone (Benoquin) used in this study was supplied by the Paul B. Elder Co., Bryan, Ohio.

3. Fitzpatrick, T. B., and Lerner, A. B.: To be published.

4. Rattner, W. H.; Lerner, A. B.; Fitzpatrick, T. B., and Wright, P. A.: To be published.

mented macule, small or large, which shows the same histological picture as a freckle. One or more *café au lait* spots may be found in approximately 10% of the population [5]; however, they may be numerous in patients with neurofibromatosis. A lentigo is a small, darkly pigmented macule that occurs on the upper parts of the body and is not related to sunlight. Histologically, there is proliferation of melanocytes at the epidermal-dermal junction; and the lesion may be considered a junctional type pigmented nevus. Lentigo senilis, or senile lentigines, are the "'liver spots" usually seen on the dorsal surfaces of the hands and arms of light complexioned persons over 50 years of age. The term nevus will be used to refer to a pigmented nevus consisting of a papule with or without hair that microscopically shows groups of benign melanocytes in the epidermis or dermis. Sharp distinctions among these diagnostic terms cannot always be drawn. For example, while some cases represent transitions between freckles and lentigines, others fall between lentigines and nevi.

CLINICAL CASES AND RESULTS

Brief case histories of the 25 patients treated for melanin hyperpigmentation are presented. Included are 12 patients with melasma, 2 with berlock dermatitis, 3 with nevi, 1 with lentigo senilis, 3 with *café au lait* spots, 2 with generalized lentigines, and 2 with freckles.‡ Of these 25 patients, 18 showed a good clinical response. Two became sensitive to the preparation, and treatment was discontinued. In one of these two patients, an excellent depigmenting response was obtained. In most of our patients treated for melasma of unknown origin and *café au lait* spots, melanin pigmentation decreased; but this was not as striking as that observed in generalized lentigines, severe freckling, berlock dermatitis, and melasma (Addision).

Patients Treated with Twenty Per Cent Monobenzyl Ether of Hydroquinone (Benoquin)

Diagnosis	No. of Patients Treated	No. of Patients Showing Improvement	No. of Patients Showing No Improvement
Melasma	39	33	6
Berlock dermatitis	5	4	1
Undiagnosed and miscellaneous melanoderma	13	9	4
Nevi	6	1	5
Lentigo senilis	1	1	..
Café au lait spot	5	4	1
Generalized lentigo	4	4	..
Freckles	5	3	2
Seborrheic keratosis	1	1	..
Congenital melanosis of eyelids	1	1	..
Benign acanthosis nigricans	1	1	..
Postinflammatory pigmentation	3	2	1
Total	84	64	20

In the table are seen the results of treatment in 84 cases of melanin hyperpigmentation, consisting of the 25 patients treated directly by us and 59 by other dermatologists, using a 20% monobenzyl ether of hydroquinone ointment locally twice daily until the desired effect was obtained. Lower concentrations were used in some instances. In addition to the 2 patients of ours in whom a sensitization reaction developed, 9 of the 59 treated by other dermatologists showed a similar response. Five of the nine patients who contracted a dermatitis showed good depigmentation. One patient, who was later given a 5% monobenzyl ether of hydroquinone, had no further difficulty.

5. (*a*) Crowe, F. W., and Schull, W. J.: To be published. (*b*) Lerner, A. B., and Fitzpatrick, T. B.: Unpublished data.

CASE 1.—A man, aged 28, had melasma of the forehead and neck of approximately five years' duration, was treated for five months with definite decrease in pigmentation, and showed no sensitization reaction.

CASE 2.—A woman, aged 33, had melasma of the face for 14 years, was treated for eight months with some decrease in pigmentation, and showed no sensitization reaction (fig. 2).

CASE 3.—A woman, aged 34, had melasma of the face for one and one-half years and was treated for seven months with definite improvement; no dermatitis developed.

CASE 4.—A woman, aged 35, had melasma of the face for about 10 years' duration, was treated for two months with some lightening of skin color, and showed no sensitization reaction.

CASE 5.—A woman, aged 59, had melasma of the arms and was treated for three months with questionable improvement; no dermatitis was noted.

CASE 6.—A woman, aged 31, had melasma (pregnancy) of the cheeks, upper eyelids, and nose, of six years' duration, was treated for four months, and showed no results and no dermatitis.

Fig. 2 (case 2).—Patient with melasma before and after eight months of therapy.

CASE 7.—A woman, aged 27, had melasma of the face of six years' duration. After one month's therapy dermatitis developed and treatment was discontinued. There was no improvement and no sensitization.

CASE 8.—A woman, aged 49, had melasma of the face. After one month of therapy, patient showed improvement and no sensitization reaction.

CASE 9.—A woman, aged 40, had melasma of the forehead and cheeks of three years' duration. After three months of therapy there was definite improvement and no dermatitis.

CASE 10.—A woman, aged 48, had melasma of the face and arms of several years' duration. The patient was treated intermittently for four months with improvement. No dermatitis developed.

CASE 11.—A woman, aged 39, had melasma of the face of five years' duration, was treated for two months with good results, and showed no sensitization reaction.

CASE 12.—A woman, aged 27, had melasma (Addison) of the face and hands, palmar creases, and mucous membranes of four years' duration; she was treated for six months, with excellent results. No dermatitis developed.

CASE 13.—A Negro woman, aged 51, had hyperpigmentation on dorsal hand surfaces for several months. The diagnosis was berlock dermatitis or heavy metal melanosis. She was treated for two months with questionable results; there was no sensitization reaction.

CASE 14.—A woman, aged 31, had berlock dermatitis of the face of one year's duration and was treated intermittently for one year with excellent results. No dermatitis was noted.

CASE 15.—A woman, aged 25, had had since birth melanoderma of the back compatible with the diagnosis of a blue nevus. There was marked depigmentation after one month of therapy. No dermatitis developed.

CASE 16.—A man, aged 27, had had since birth a flat pigmented nevus approximately 6 cm. in diameter on the left side

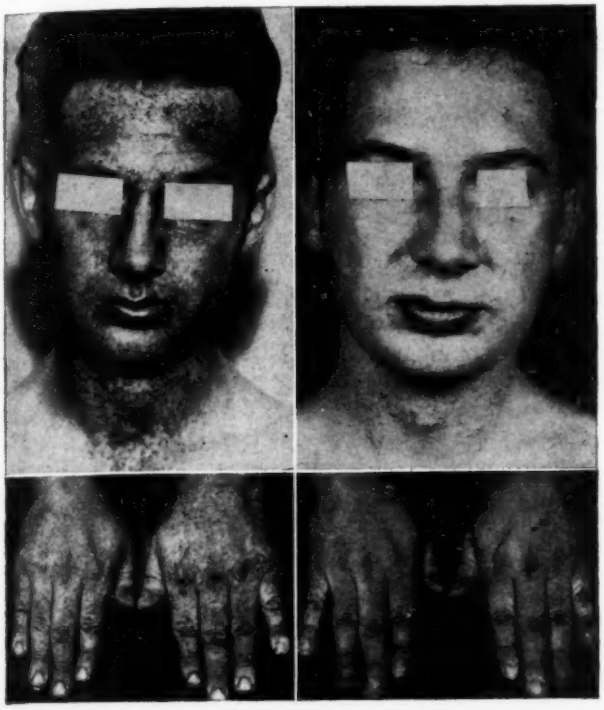

Fig. 3 (case 23).—Patient with generalized freckles and lentigo before and after 20 months of therapy for the face and neck and 5 months for the hands.

of the face. After four months of therapy there was a questionable decrease in pigmentation and no reaction to the drug.

CASE 17.—A woman, aged 24, had a pigmented nevus on arm since childhood and was treated for four months. No change and no sensitization were noted.

CASE 18.—A woman, aged 65, had lentigo senilis on dorsal surfaces of the hands and arms, was treated for two months with definite improvement, and showed no sensitization reaction.

CASE 19.—A woman, aged 21, had a *café au lait* spot on the arm since childhood and was treated for three months, with decrease in pigmentation of the lesion. No dermatitis developed.

CASE 20.—A girl, aged 16, had a *café au lait* spot on the arm present since birth; after four months' treatment, there was some lightening of the hyperpigmented area and no sensitization reaction.

CASE 21.—A woman, aged 54, had a *café au lait* spot on the cheek most of her life; she showed marked improvement after four months' treatment. No dermatitis developed.

CASE 22.—A man, aged 25, had generalized lentigines and was treated intermittently for one year with slight improvement. No sensitization was noted.

CASE 23.—A man, aged 28, had marked generalized lentigines and freckles since early childhood with severe secondary neurosis because of the disfigurement. His face, neck, and hands were treated for two years with 33% monobenzyl ether of hydroquinone and then for one year with the 20% ointment. Almost complete disappearance of lesions occurred. No dermatitis developed (fig. 3).

CASE 24.—A girl, aged 19, had freckles of exposed areas since childhood. Her face and hands were treated for two months with striking improvement. At the end of this period, the patient stated that irritation had developed on applying the drug. She discontinued treatment, and the excellent cosmetic results remained (fig. 4).

CASE 25.—A woman, aged 28, had numerous freckles on the face and neck since childhood, was treated with 5% monobenzyl ether of hydroquinone for two months with marked improvement, and showed no sensitization reaction.

FEASIBILITY OF COMPLETE BODY DEPIGMENTATION

Since monobenzyl ether of hydroquinone is an effective depigmenting agent when prepared and used properly, a question commonly asked is whether or not it is possible to remove all the pigment from the skin of a darkly pigmented person. In general the preparations reported herein cannot be used for this purpose unless a concentrated effort is made over a long period of time. Even so, results would be questionable; however, in certain special cases complete depigmentation may be practicable, as in patients with vitiligo or those predisposed to this disorder. Evidence from various sources indicates that monobenzyl ether of hydroquinone is much more effective in patients with vitiligo than in persons with normal skin. Two Negro patients who had disfiguring vitiligo of the face and body used these preparations on a single arm for long periods of time and became completely depigmented, except for the hair and eyes, which retained their normal coloring.[6] One of these patients became pregnant after she was depigmented but still receiving treatment. She gave birth to a normally colored baby. Hence, locally applied monobenzyl ether of hydroquinone does not affect the skin color of the fetus in utero. In a third Negro total vitiligo developed and later began to repigment with small unsightly spots.[7] She prevented

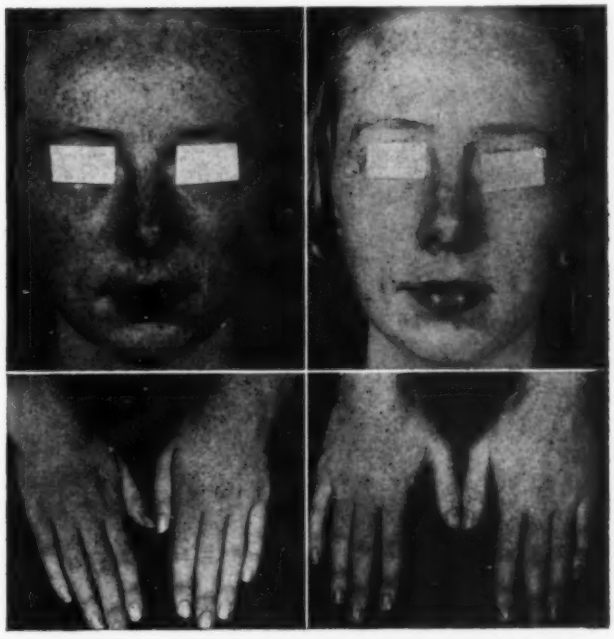

Fig. 4.—Patient with freckles before and after two months of therapy.

appearance of these spots by applying ointments containing monobenzyl ether of hydroquinone. In a fourth Negro who had slight vitiligo extensive vitiligo developed

6. Stolar, R.: Personal communication to the authors.
7. Schwartz, L.: Personal communication to the authors.

following local depigmentation of the legs from a rubber garter, which probably contained monobenzyl ether of hydroquinone.[8] None of the patients showed depigmentation of the hair or eyes. This may be an indication that monobenzyl ether of hydroquinone does not act directly on the melanocytes but is first converted in the skin to another substance. No knowledge is available on the effect of this medication orally on pigmentation in human beings. In white patients with malignant melanomas treated by Kelly, Bierman, and Shimkin [9] with oral monobenzyl ether of hydroquinone obvious changes in pigmentation did not develop.

In our experiments [§] with five normal Negro subjects, 20% monobenzyl ether of hydroquinone was applied daily to one arm for two months without change in pigmentation; however, one subject readily underwent depigmentation in one month on covering the site of application of the ointment with gauze and adhesive tape. Repigmentation was complete two months later. Similar results were obtained when the 5% monobenzyl ether of hydroquinone was used in the same subject.

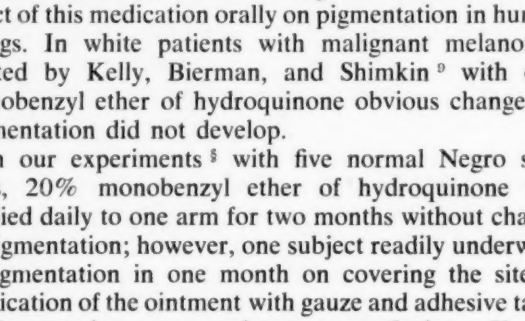

Fig. 5.—Results of continuous patch tests on back of Negro male volunteer for one month. Ten per cent monobenzyl ether of hydroquinone was used on the left and 30% on the right.

THERAPEUTIC PREPARATIONS AND METHOD OF TREATMENT

The purity and concentration of monobenzyl ether of hydroquinone and the vehicle and mode of application are important factors in obtaining a good clinical result. It is possible that early work with monobenzyl ether of hydroquinone was associated with sensitization reactions because of the presence of about 10% contaminants. This crude preparation contained dibenzyl ether of hydroquinone and unidentified oxidation products. In addition, the physical state of the material was such that its incorporation in an ointment resulted in a gritty mixture that abraded the skin. The ointment (Benoquin) used in our studies consisted of purified and finely milled monobenzyl ether of hydroquinone.

Patch tests on the skin of normally colored persons [10] showed that the greater the concentration of the drug in the ointment, the more rapid the depigmentation. For example, as shown in figure 5, a 30% ointment was more effective than a 10% ointment; however, almost any concentration from less than 1% to 50% was effective, depending on the frequency of application and unknown factors peculiar to the person. Occupational and accidental depigmentation from rubber gloves, other rubber items, and adhesive tape was obtained with only small quantities of monobenzyl ether of hydroquinone. Some dermatologists prefer a 5% ointment. Most of the patients followed by us were given a 20% ointment, but in some cases the concentration of the drug was 5%. If a given concentration produces a dermatitis, the concentration should be decreased. If necessary, the material should be applied less frequently rather than discontinuing treatment. Stolar [6] and Horne [11] obtained good therapeutic results in patients sensitive to the drug by adhering to these procedures.

Many substances have been suggested as vehicles in which to incorporate monobenzyl ether of hydroquinone for local application, including organic solvents (or mixtures) of acetone, alcohol, and olive oil; ointment bases of petrolatum or water washable substances; pomade sticks; and plaster. Oral use of the drug has been considered. All locally applied preparations, except sticks, which were not tried, can bring about depigmentation. The ointment bases, particularly those that are water washable, are the easiest to use. Alcohol or acetone preparations are too drying for many patients, and olive oil is too greasy. Good results were obtained with 10% monobenzyl ether of hydroquinone plaster in two out of four patients with *café au lait* spots and one Negro serving as a control after three to eight weeks' therapy; however, in two of the patients a dermatitis developed after three weeks' application of the plaster.

As mentioned earlier, although oral preparations were not tried, the drug is not toxic; and depigmentation by this method must be studied. Grupper [12] stated that parahydroxypropiophenone, used orally or locally, could bring about depigmentation but that the combination of both forms of therapy was most effective. Monobenzyl ether of hydroquinone should be investigated for possible similar results.

Ointment preparations are applied to the skin twice daily until depigmentation appears, usually in one to three months. After obtaining the desired depigmentation, applications are reduced to once daily and later once weekly. At times transient burning of 5 to 20 minutes' duration occurs after the ointment is applied. This reaction does not indicate cessation of therapy because symptoms usually disappear after three weeks' use. If a dermatitis develops after application of the ointment, the preparation should be diluted to 1 to 5% and, if necessary, applied less frequently than twice a day. The treatment of a patient in whom sensitivity to the drug develops cannot be clearly outlined but must be managed individually by the physician.

RATE AND DURATION OF DEPIGMENTATION

The rate of depigmentation of a treated pigmented area varies greatly, ranging from three weeks to six months. As stated previously, the concentration of the active agent and the mode of application, as well as factors peculiar to the person, are important. Adhesive tape or other types of occlusive covering over the ointment-treated areas result in more rapid and complete depigmentation; however, it is not practical to cover areas such as the face for long periods of time, and these are the regions for which the patient usually seeks treatment.

8. Perry, T.: Personal communication to the authors.

9. Kelly, K. H.; Bierman, H. R., and Shimkin, M. B.: Negative Effects of Oral Monobenzyl Ether of Hydroquinone in Malignant Melanoma in Man, Proc. Soc. Exper. Biol. & Med. **79**: 589, 1952.

10. Denton, C. R.; Lerner, A. B., and Fitzpatrick, T. B.: Inhibition of Melanin Formation by Chemical Agents, J. Invest. Dermat. **18**: 119, 1952.

The more concentrated the preparation, the more rapid the rate of depigmentation (fig. 5).

When ointment preparations of monobenzyl ether of hydroquinone are used to treat freckles, lentigo, and melasma, no change occurs in the normally pigmented skin of the fingers used to apply the medication or in the areas contiguous to those of hyperpigmentation. An albinic color is not obtained. An exception was a Negro woman with melasma (pregnancy) in whom localized leukoderma of the face developed after the application of a 5% ointment.[13] Pigmentation returned when therapy was discontinued. It is an interesting phenomenon that, whereas in white patients normal skin pigmentation is not affected, in Negroes not only the abnormally pigmented areas disappear but also the pigment of normal skin. Hence, there is a difference in the total net effect of local application of monobenzyl ether of hydroquinone on Negro and on white skin. Some unknown balance between melanin formation and melanin depletion may operate to explain this phenomenon. In short-term (30 day) tests [10] on Negro patients, no correlation was found between the intensity of their pigmentation and the rate of depigmentation.

The rate of repigmentation after complete cessation of therapy varies from two months to periods of unknown duration. Some patients with occupational leukoderma related to monobenzyl ether of hydroquinone did not regain normal pigmentation. In all our patch test studies with Negroes pigmentation was complete within three months. In patients with freckles and melasma, exposure to sunlight increased the rate of repigmentation. Such patients must be instructed to avoid overexposure to sunlight. Ultraviolet light protective agents are sometimes useful.

MECHANISM OF ACTION

Experimental work has shown that monobenzyl ether of hydroquinone has no action on melanocytes or the tyrosine-tyrosinase reaction, but it may be split to form hydroquinone, which in turn inhibits melanin formation.[10] Fassett [14] believes that this hypothesis is incorrect and that hydroquinone does not affect pigmentation. Whereas persons who handle hydroquinone do not become depigmented, those who work with monobenzyl ether of hydroquinone occasionally do; however, it is known that parenteral administration of hydroquinone produces depigmentation in experimental animals. Hydroquinone is a good inhibitor of the tyrosine-tyrosinase reaction.[10] Inhibition of a metabolic process depends on the presence of an active agent at a specific site. It is possible that hydroquinone does not reach the melanocyte on application to the skin and that monobenzyl ether of hydroquinone is converted at the proper site in the skin to hydroquinone, which in turn can inhibit melanin formation.

OTHER DRUGS

Para-hydroxypropriophenone is the only substance similar to monobenzyl ether of hydroquinone that has been used to effect depigmentation. Both chemicals are parahydroxyphenyl derivatives. Para-hydroxypropriophenone has been used locally and orally in the treatment of melasma (Riehl).[15] Best results were obtained with 1 to 2 gm. of the drug orally daily and a 12% ointment locally. This drug has not been used extensively by us. No depigmentation occurred in Negro patients with patch tests performed similarly to those with monobenzyl ether of hydroquinone that produced depigmentation.[10]

Ointments containing ammoniated mercury have been, and are continuing to be, used for removing freckles. The results have been inconsistent. Even when an effect is attained, it is weak and not clear-cut.

At the present time much is known about melanin formation,[1] including the type of cell (melanocyte), the substrate (the amino acid tyrosine), the enzyme (tyrosinase—a copper protein complex), and the chemical steps involved in this process. Because of this knowledge, new methods may be found to inhibit melanin formation; however, at this date, monobenzyl ether of hydroquinone remains the most effective and useful agent.

SENSITIZATION AND TOXICITY

The only toxic reaction to monobenzyl ether of hydroquinone has been sensitization with subsequent dermatitis. No systemic toxicity has been observed. As a patch test, the 20% ointment containing purified monobenzyl ether of hydroquinone was applied to the forearm of 260 normal persons for 48 hours.[10] Three persons (1.2%) showed a mild reaction consisting of localized erythema and edema. Similar testing, using an ointment of 20% crude monobenzyl ether of hydroquinone on 90 persons, resulted in mild reactions in 3 cases (3.3%). Retesting the purified preparation on 135 persons three weeks after the initial experiment revealed no new instances of reactions; however, on retesting the crude preparation on 76 persons, it was found that 3 reacted (4.0%). Thus it appears that the purified monobenzyl ether of hydroquinone is less sensitizing than the crude chemical; however, a greater series of cases would have to be studied to establish this point.

Of 31 persons, including patients and test subjects who applied the ointment for two months under our direct supervision, 2 showed sensitivity to the drug. In one of these (case 2), an excellent clinical result was obtained before sensitivity appeared. Of 59 patients treated by other dermatologists, 9 showed sensitization reactions. Five of the nine patients showed good clinical results, and one maintained a good effect without the development of dermatitis when 5% monobenzyl ether of hydroquinone was used instead of 20%. As mentioned earlier, the plaster preparations produced a localized dermatitis in two out of five cases although the clinical responses were good in that depigmentation occurred. One of our patients (case 23) used various preparations of monobenzyl ether of hydroquinone over the entire face, neck, and hands daily for almost three years. During the past year, he used only the 20% formula. Clinical and laboratory findings were completely normal.

It is interesting that approximately 13% of patients treated with 20% purified monobenzyl ether of hydroquinone showed some type of sensitization, whereas only 1.2% of persons patch-tested with the same ointment reacted on initial testing. No reactions were seen on retesting three weeks later. It can be concluded that patch testing alone does not simulate therapeutic use of these preparations in regard to the development of sensitization. The ointments are diluted from 20 to 5% if their

application results in transient burning or erythema. Stolar [6] and Horne [11] obtained good clinical results in patients sensitive to the drug by diluting the preparations and applying them less frequently.

Kelly, Bierman, and Shimkin [9] administered monobenzyl ether of hydroquinone to eight patients with malignant melanomas. Total doses of 2.9 to 1,490 gm. administered in daily amounts of 0.5 to 25 gm. orally for 21 to 214 days produced no toxic effects other than transient nausea and vomiting when the daily dose exceeded 10 gm. The growth of the melanomas was not affected. Seven of the eight patients died after an expected course of their malignancy. Necropsy of these seven failed to reveal histological evidence of toxic effects or other changes attributable to ingestion of the drug. No toxic changes were observed in mice receiving 600 mg. per kilogram of body weight of monobenzyl ether of hydroquinone intraperitoneally daily for three weeks [5b] or in guinea pigs ingesting 160 mg. per kilogram daily for two months.[10]

SUMMARY

Of 84 patients with increased melanin pigmentation treated with 20% monobenzyl ether of hydroquinone (Benoquin), 64 showed a good clinical response after two to six months' treatment. Eleven of the 84 patients (13%) became sensitive to the ointment and reported a local dermatitis; however, 7 of these 11 patients had an excellent therapeutic effect before the sensitivity was acquired.

Results obtained on patients treated directly by us showed monobenzyl ether of hydroquinone to be highly effective in generalized lentigines, severe freckling, hyperpigmentation due to photosensitization following use of certain perfumes (berlock dermatitis), and melasma (Addison). Treatment was moderately successful in melasma (pregnancy) but of little or no value in *café au lait* spots or pigmented nevi. Other physicians reported good results in melasma (pregnancy) and postinflammatory hyperpigmentation but only fair improvement of *café au lait* spots. Mild or moderate freckling should not be treated because these lesions usually fade spontaneously during the winter months and the incidence of sensitization to the drug is relatively high.

The feasibility of complete body depigmentation was discussed. Factors relative to therapy such as concentration of the drug, type of vehicle, mode of application, duration of treatment, and management of patients with sensitivity were considered.

MECONIUM PERITONITIS

Herbert M. Olnick, M.D.
and
Milford B. Hatcher, M.D., Macon, Ga.

Meconium peritonitis is an aseptic chemical peritonitis that follows perforation of the intestines in fetal life. Although this condition is infrequent, it should be emphasized that the correct diagnosis can be made on the basis of characteristic roentgenographic findings. This is of considerable clinical importance in the surgical differential diagnosis of acute abdominal conditions in infancy. A case of meconium peritonitis with the unusual presenting complaint of scrotal swelling is described as well as a typical case.

Simpson [1] is credited with the first comprehensive presentation of meconium peritonitis in 1838, in which he reviewed 15 cases and added 9 of his own. By 1949 over 100 cases had been reported in the literature.[2]

Occurrence of this disease requires the presence of fetal peristalsis and meconium, both of which make their appearance during the second trimester of prenatal life. Boikan [3] cites Rudnew's case of a stillborn fetus of six months' development that had meconium peritonitis with calcification. When, as in our case 1, a definite obstruction of the intestines can be demonstrated, the pattern of events—hyperperistalsis, thinning of the wall, and perforation—is readily understood. In other instances, weakness of the wall or abnormal meconium is predicted as the prime factor.

Meconium is a sterile mixture of cast off epithelial cells, bile, fats, stearic acid, sebaceous material from swallowed amniotic fluid, mucin, and salts. When the meconium enters the peritoneal cavity, it creates a vigorous irritation and gives rise to a tremendous adhesive process. Calcification occurs at varying intervals from the time of perforation and is usually demonstrated overlying the epithelial cells in the exudate. If the intestinal perforation occurs at or near the birth of the baby, surgical exploration will reveal bile, meconium, and probably free air in the peritoneal cavity. If the original perforation occurred earlier, extensive adhesions and calcification will be present (fig. 1*A*).

In 50% of the cases of meconium peritonitis, definite obstructive lesions to the wall of the intestine can be demonstrated, such as volvulus, intussusception, congenital bands, angulation and kinks, atresia, and stenosis; the latter two lesions are seen most commonly. When a low large bowel obstruction results in perforation, the tear may be found in more than one place and anywhere from the sigmoid to the cecum.[3] The commonest location of perforation in the small bowel is approximately 10 cm. proximal to the site of obstruction. Small intestinal stenoses and atresias are commonest in the duodenum and ileum. When found in the duodenum, they are usually single, and when found in the ileum, they are not

Dr. H. S. Weens assisted in the study of these patients.

From the Department of Radiology, Emory University School of Medicine, Atlanta, Ga., and Middle Georgia Hospital, Macon, Ga.

1. Simpson, J. Y.: Meconium Peritonitis in the Fetus in Uterus, Edinburgh M. J. **15**: 390-414, 1838.

2. Low, J. R.; Cooper, G., Jr., and Cosby, L., Jr.: Meconium Peritonitis, Surgery **26**: 223-228, 1949.

3. Boikan, W. S.: Meconium Peritonitis from Spontaneous Perforation of the Ileum in Utero, Arch. Path. **9**: 1164-1183 (June) 1930.

uncommonly multiple. The bowel distal to an atresia will usually be collapsed, owing to the fact that meconium has never passed through it.[4]

Conditions other than those obstructing the wall of the intestine can produce perforation. Meconium ileus, congenital diverticula, ulcers and hyperplastic lymph and glandular tissue have been incriminated as factors producing weakening of the wall and rupture in various cases. The role of trauma has not been established.[3]

The existence of the fetus is endangered even before birth by polyhydramnios and by dystocia in labor due to distention of the abdomen and to edema of the abdominal wall of the fetus. The newborn infant is usually acutely ill and cyanotic, vomits frequently, and has absent or scanty stools. At times blood may be present in the stools and vomitus.

X-ray examination is helpful. Distention of the small bowel points to the presence of intestinal obstruction. If the perforation is recent, free air may be demonstrated on upright films of the abdomen. If the perforation has taken place at some previous date, a characteristic streaky and plaque type of calcification may be seen distributed throughout the entire peritoneal cavity, frequently extending over the dome of the liver.[5]

Recent articles have described intraluminal calcifications of a stippled appearance associated with intestinal atresia, in which instances the preoperative roentgenogram misled the radiologist into an interpretation of meconium peritonitis. At operation the peritoneum was clear and the densities were all part of the intestinal contents. This condition may be differentiated on the roentgenogram by the central location of the densities in contrast to the involvement of the parietal peritoneum of the abdominal wall and liver areas in meconium peritonitis.

Surgical treatment is the only recourse in the acutely ill infant. Not only must the underlying lesion causing the perforation be relieved and the perforation closed but the operator is faced with resecting the tremendous number of adhesions that are present in order to expose the lesion. The postoperative course is complicated by these adhesions, which promptly reform and which present the hazard of a recurrent obstruction. Despite the poor outlook, in at least three cases recorded in the literature the patients have recovered following surgery.[6] Following is a description of two instances of meconium peritonitis that have been encountered during the past few years.

CASE 1.—A white baby girl was born on April 24, 1952, following a normal delivery by Dr. O. R. Thompson. The only sibling is normal. The patient's abdomen was somewhat distended. No other abnormality was noted at birth.

During the first few hours of life, the abdomen increased in size and the child became restless. The surgical consultant saw this child at 18 hours of age. Marked distention and dyspnea were noted and seemed to indicate a congenital intra-abdominal gastrointestinal anomaly. A scout film of the abdomen was ordered.

The roentgenologist reported considerable abdominal distention from a distended small bowel and peritoneal fluid. Calcifications were noted throughout the entire peritoneal cavity, extending over the dome of the liver. The barium enema examination revealed the colon to be patent throughout but of small caliber. Barium given orally failed to enter the duodenum. The close relationship of the gas-filled small intestinal loops in the anterior superior portions of the abdomen was felt to be due to the adhesive and calcific peritonitis. Meconium peritonitis with small intestinal atresia was the preoperative roentgenographic diagnosis (fig. 1).

Laparotomy was done 20 hours after birth through a right rectus incision. The peritoneal cavity was completely filled with a dark green, somewhat mucoid-looking fluid, which was aspirated. The peritoneum and the abdominal viscera were thickened by a dark bluish-black membrane, apparently old meconium, which made the bowel appear to be gangrenous.

When this membrane was removed, the underlying intestines appeared viable. The stomach and duodenum were markedly dilated and thickened (6 mm.) from hypertrophy of the wall secondary to an obstructive thickening in the area of the ligament of Treitz, the exact nature of which could not be determined.

The main finding was an atresia, 1 in. (2.5 cm.) in length, of the distal ileum just proximal to the ileocecal valve. Just above the atresia the ileum was ruptured, and normal-appearing meconium was exuding from the lumen. A small rubber catheter was inserted into the small intestine, and irrigation with isotonic sodium chloride was done to remove as much meconium as possible.

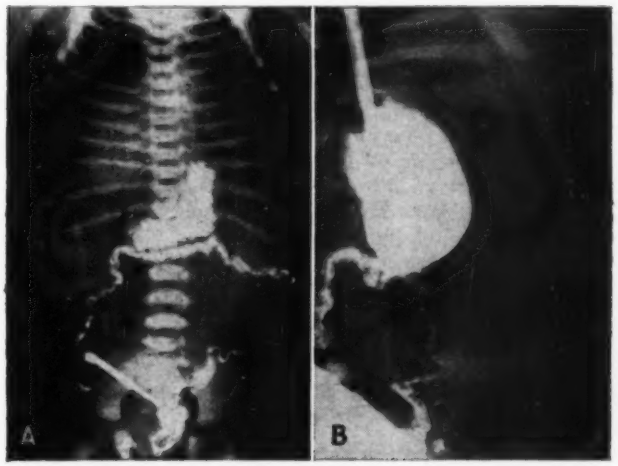

Fig. 1 (case 1).—*A*, meconium peritonitis following ileal atresia. The stomach and underdeveloped colon are outlined with barium. Note the widespread calcifications in the abdomen. *B*, lateral view. Note the collection of gas in the small bowel loops, which form a cluster from the matted adhesions. (The white streak in the center is a film scratch.)

An ileocecostomy to bypass the atresia was performed. When the large bowel was opened, residual barium from the preoperative colon study was found. Meconium was absent. An interesting finding at operation was the lighter color of the colon, which helped to distinguish the large bowel. The difference was due to the absence of meconium in the colon and the presence of barium remaining from the enema examination. The obstruction around the ligament of Treitz was bypassed by a gastroenterostomy. The abdomen was anatomically closed.

The patient stood the operation well and the next day appeared to be progressing. Blood, penicillin, and fluids parenterally were administered. Three days following surgery, the patient had a bowel movement and the abdomen was fairly soft. The Wangensteen suction was discontinued, and water was given by mouth.

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4. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941, pp. 25-52.

5. Neuhauser, E. B. D.: The Roentgen Diagnosis of Fetal Meconium Peritonitis, Am. J. Roentgenol. **51**: 421-425, 1944.

6. Conrad, H. A., and Robbins, F. R.: Congenital Atresia of the Jejunum with Meconium Peritonitis, J. Internat. Coll. Surgeons **15**: 320-327, 1951. Low.[3] Neuhauser.[5]

Five days following surgery, she was given a formula. Two days after a formula was given, the patient began to vomit and her abdomen became distended. The temperature rose, and diarrhea developed. Nine days postoperatively, a fistula developed, and the wound broke down. She continued a downhill course and died on the 13th postoperative day. Permission for an autopsy was not obtained.

This is a fairly typical case of meconium peritonitis secondary to an ileal atresia, which apparently perforated in prenatal life and was still patent at the time of surgery on the first day of life. The x-ray findings in this case were characteristic, and the diagnosis was made preoperatively.

CASE 2.—A two-month-old Negro boy was admitted to Grady Memorial Hospital on Dec. 12, 1947, with a chief complaint of enlargement of the scrotum. This child had a normal delivery and weighed 7 lb., 8 oz. (3,402 gm.) at birth. Tests of the mother's blood for syphilis were negative.

At the time of delivery the scrotum was noted to be markedly swollen. In the two months since birth the scrotum had diminished to one-half its previous size but was still three to four times normal size. The child was asymptomatic in every other respect and was gaining weight normally. There were no other physical findings except for the enlarged scrotum. Results of laboratory studies, which included determination of the blood calcium, serological studies, and duodenal trypsin studies, were noncontributory. The suggested clinical diagnoses included bilateral epididymitis and orchitis, syphilitic orchitis, teratoma, and bilateral hydrocele.

Intravenous urography revealed numerous mottled and stippled areas of calcification in both sides of the scrotum in the deep tissues surrounding the testicle and epididymis (fig. 2). One of the radiologists (Dr. E. T. Walker) noted numerous areas of calcification within the confines of the peritoneal cavity extending above the dome of the liver (fig. 3). Roentgenographic studies of the entire body revealed no other areas of calcification. The conclusion was that this child had had a perforation of the intestine during fetal life resulting in spillage of meconium into the peritoneal cavity, with spontaneous sealing of the opening. The clinical and x-ray findings were the residual changes of meconium peritonitis, which occurred during fetal life when the main peritoneal cavity and the processus vaginalis to the scrotum freely communicate. Normally this communication ceases within a few weeks to a few months after birth.[7]

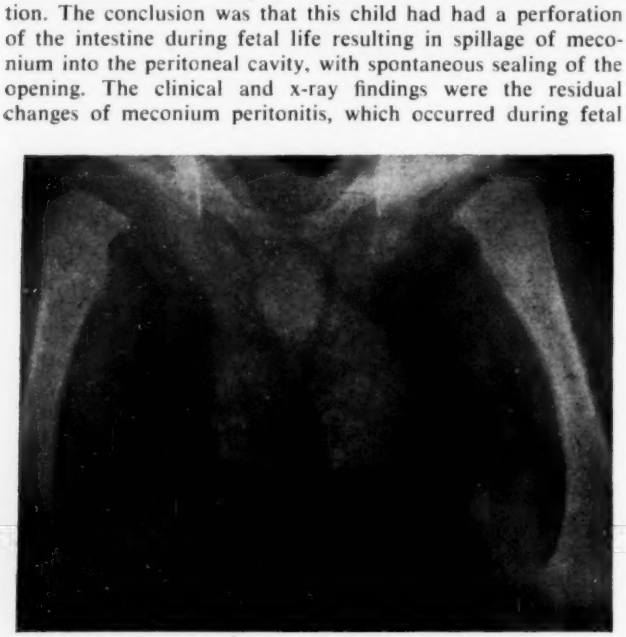

Fig. 2 (case 2).—Bilateral peritesticular calcification secondary to meconium peritonitis in a two-month-old infant. Note the scrotal enlargement.

7. Arey, L. B.: Developmental Anatomy, ed. 3, Philadelphia, W. B. Saunders Company, 1934, p. 271.

A biopsy of the testicular mass was performed on Jan. 9 at 2½ months of age and showed "loose fetal connective tissue with slight acute and chronic inflammatory cell infiltration and some areas of calcification." Follow-up clinical examination in the outpatient department up to the present time has revealed no further trouble except for one brief episode of scrotal swelling, which quickly subsided. A repeat roentgenogram taken in August, 1952, at 5 years of age showed considerable diminution in the amount of calcification.

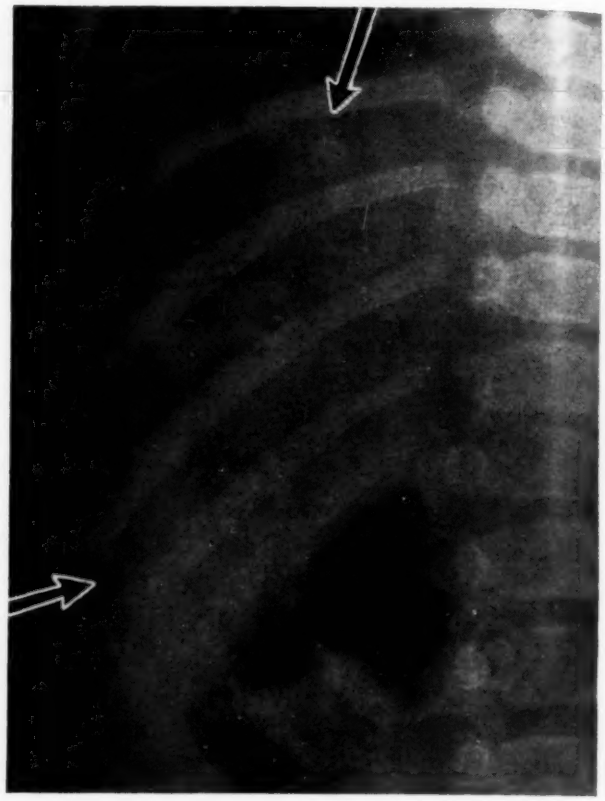

Fig. 3 (case 2).—The arrows indicate calcifications of peritoneum in liver area.

This case is unique in that the child had no intestinal symptoms and was hospitalized because of scrotal swelling. The basis of the scrotal abnormality was described by Simpson [1] in case 4 of his original presentation. "Both the tunicae vaginales of the testes still communicated with the cavity of the peritoneum and the serous surface of the left one was partially coated by a layer of coagulable lymph." No known disease entity other than meconium peritonitis can account for these calcific foci in the scrotal, abdominal, and liver areas of our patient.

SUMMARY

The disease entity, meconium peritonitis, is reviewed, and a typical case is described. A case of scrotal enlargement with calcification in the peritesticular tissues and with calcifications in the peritoneal cavity, all believed due to meconium peritonitis in prenatal life, is also described. This second case is unusual because the child is completely asymptomatic as far as the intestinal tract is concerned. This is the first case on record of meconium peritonitis causing calcification in the scrotum.

Rm. 417, Persons Bldg. (Dr. Olnick).

CLINICAL PROBLEMS RELATING TO THE MANAGEMENT OF INFECTIONS WITH ANTIBIOTICS

Wesley W. Spink, M.D., Minneapolis

Any physician who was responsible for patients with bacterial infections prior to the introduction of the sulfonamides and the antibiotics can readily appreciate the advantages that these therapeutic agents have brought about in the management of infectious diseases. One could dwell at length on the change in the clinical pattern that has resulted from modern antibiotic therapy in each of several infectious diseases. Consider the natural course of untreated hemolytic streptococcic septicemia, with its previous mortality of over 75% as compared to that of less than 10% existing today because of these advances in treatment. Gonorrhea can be successfully treated overnight, and no longer are hospital beds filled with patients having debilitating and chronic complications resulting from this venereal disease. Some of the most remarkable therapeutic triumphs involve patients with such diseases as subacute bacterial endocarditis or pneumococcic meningitis, in which recovery of an untreated patient is extremely rare.

Although revolutionary advancements have occurred in the management of infectious diseases, the clinician is often perplexed by those infectious processes that fail to respond favorably to the antibiotics; paradoxically, the antibiotics have brought forth new clinical problems. At this point it is well to review some of the unsolved clinical problems in the management of infectious diseases and to consider some of the disadvantages induced by the widespread use of the antibiotics.

SOME PROBLEMS CREATED BY ANTIBIOTIC THERAPY

One or two basic therapeutic principles should govern the clinician in his use of the antibiotics. Either as a result of precise laboratory data or on the basis of adequate clinical experience, he can decide that a given patient is suffering from a specific infectious disease. Oftener than not information is available to determine whether an antibiotic is indicated in such a disease; if so, the antibiotic should be used that has been shown to be the most effective. Unfortunately, as simple and as sound as these principles are, many clinical problems are created by the indiscriminate use of the antibiotics in such situations. A current pernicious therapeutic philosophy is based on the following conclusions: 1. The antibiotics are highly effective for many common bacterial infections. 2. These drugs are readily available, inexpensive, easy to administer, and relatively nontoxic. 3. In cases in which the patient is febrile with the cause in doubt, before investigating the basic causes of the illness, therapy with an antibiotic should be attempted. In some instances a seriously ill patient is benefited by such a procedure, but in too many cases such an approach not only curtails the arrival at a correct diagnosis but may actually jeopardize the eventual recovery of a patient. A widespread epidemic of respiratory diseases, including influenza, occurred during the winter of 1952-1953. In this community many persons, with and without the advice of physicians, took one or more antibiotics. In some instances suppurative complications may have been prevented by such medication, which was desirable in selected groups of patients. But in the majority of treated cases the clinical course was unaltered; a false sense of security dominated the patients — and physicians; the antibiotics induced troublesome, and even disabling, side-effects; occasionally, a more serious febrile disease than a mild respiratory disease was masked by such therapy.

It should be emphasized that most of the viral infections, many fungus diseases, and some bacterial infections are not benefited by antibiotic therapy. Whenever possible, and particularly in the seriously ill patient, every effort should be made to define the etiological agent responsible for an infection. The indiscriminate use of antibiotics in patients not only may destroy readily available bacteriological evidence as to the nature of the disease but may leave the attending physician with a patient who remains febrile and ill in spite of treatment with an antibiotic. This has occurred many times in instances of subacute bacterial endocarditis. In this disease, the micro-organism should be isolated and in vitro sensitivity test carried out, so that the proper antibiotic or combination of antibiotics can be selected and intensive treatment utilized for several weeks. Every staff in a large general hospital has encountered situations in which febrile patients with lymphoblastomas, blood dyscrasias, infectious mononucleosis, or malignant lesions have been uselessly treated with a variety of antibiotics before it was decided to seek out the fundamental causes for the illness.

One of the remarkable features of the antibiotics is that these agents exert their antibacterial effects by altering the metabolic activity of the bacterial cells but have little or no associated deleterious action on the cells of the host. Nevertheless, these drugs do cause side-effects, which may be more serious than the disease for which they are being prescribed. At least 1 to 2% of patients to whom penicillin is administered manifest hypersensitivity to the antibiotic. These reactions vary from a mild febrile response with or without a skin eruption to a violent systemic illness that simulates serum sickness. Rarely are these drug reactions irreversible and so progressively severe that death ensues. I have witnessed two, and possibly three, cases of fatal periarteritis nodosa where penicillin appeared to be the cause. Streptomycin also induces manifestations of hypersensitivity such as fever, skin rashes, and purpura. In addition, damage to the eighth nerve may occur owing to streptomycin, which provokes vestibular dysfunction, and dihydrostreptomycin may cause varying degrees of loss of hearing. These deleterious effects on the eighth nerve can be reduced by

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combining equal parts of streptomycin and dihydrostreptomycin. In my experience, the so-called broad spectrum antibiotics, aureomycin and oxytetracycline (Terramycin), rarely cause hypersensitivity reactions in the form of fever and skin eruptions; but these agents may initiate disturbing side-effects referable to the gastrointestinal tract. Common manifestations are nausea, vomiting, abdominal distress, and, at times, diarrhea. The bacterial flora of the intestinal tract can be markedly altered by the ingestion of these agents, with the suppression, and even the elimination, of many species of bacteria. On the other hand, whereas the growth of some bacteria is suppressed, there are other species of microorganisms that reproduce more rapidly under these circumstances. The appearance of large numbers of fungi, like Candida, may result in inflammatory reactions involving the intestinal tract from the oral mucosa to the rectum. In a few instances, especially where the patient is poorly nourished, there may be a systemic invasion of the tissues by Candida fungus. At times profuse diarrhea may ensue, and some patients have exhibited the clinical features and lesions of acute ulcerative colitis. A severe form of diarrhea with dehydration and shock may be associated with the rapid multiplication of resistant staphylococci that produce an enterotoxin.[1] Examination of the stools will reveal an almost pure culture of Micrococcus pyogenes. Less violent effects on the gastrointestinal tract have been attributed to chloramphenicol, but this antibiotic may have a severe depressing effect on the bone marrow, resulting in an irreversible and fatal aplastic anemia. In regard to the gastrointestinal disturbances induced by the antibiotics, any of the antibiotics when administered orally may be potential offenders. Bacitracin, polymyxin, and neomycin are all nephrotoxic agents and should be used with extreme caution for systemic purposes. In addition, neomycin is ototoxic. Neomycin has been used extensively, without undesirable reactions, in the University of Minnesota clinics for the preoperative preparation of patients who undergo surgery on the gastrointestinal tract. Furthermore, neomycin has been employed in aerosol form by Waisbren and Hall [2] for bronchiectasis, chronic bronchitis, and lung abscess. No toxic reactions have followed the use of 0.5 gm. in 3 ml. of sodium chloride solution administered with a no. 40 DeVilbiss nebulizer twice daily. Aside from gastrointestinal disturbances, no serious reactions have thus far been attributed to erythromycin and carbomycin.

Reference has already been made to the emergence and proliferation of strains of bacteria highly resistant to the antibiotics as a result of the selective action of these agents. Some aspects of this problem will be developed in more detail shortly. Of major concern is the dissemination of strains of staphylococci that not only are resistant to penicillin, streptomycin, aureomycin, oxytetracycline, and chloramphenicol but are also beginning to manifest resistance to some of the newer antibiotics.

1. Fatal Enterotoxic Reactions Caused by Antibiotic Therapy, editorial, Minnesota Med. 36: 63, 1953.

2. Waisbren, B. A., and Hall, W. H.: Personal communication to the author.

3. Weinstein, L.: The Spontaneous Occurrence of New Bacterial Infections During the Course of Treatment with Streptomycin or Penicillin, Am. J. M. Sc. 214: 56, 1947.

Another problem involves the resistance of many species of gram-negative bacteria to penicillin. The clinicians may properly start treating an infection due to a susceptible strain of gram-positive organisms and then, because of the overgrowth of a resistant strain or strains of gram-negative bacteria, end treating a new bacterial infection in the patient as a result of penicillin therapy. A similar sequence of events has occurred in cases in which streptomycin was used and an infection due to gram-positive organisms appeared later.[3]

CHOICE AND COMBINATIONS OF ANTIBIOTICS

Reflecting the competitive nature and resourcefulness of the pharmaceutical industry, hundreds of antibiotics have been investigated as potential therapeutic agents. Fortunately, relatively few of them have been placed at the disposal of the physician. Those organizations that have uncovered a new and acceptable antibiotic have exploited their good fortune by pinpointing the efforts of the whole sales force on their new agent, always fearful in the meantime that another more desirable antibiotic of their competitors will be marketed. Those companies that have not discovered their own antibiotic have often launched an altered form of an established antibiotic, such as penicillin, or a combination of antibiotics, and some have even found it profitable to place a revised form of a sulfonamide before the medical profession. It is little wonder that the bewildered physician, besieged by detail men, attractive literature, and the voluminous reports in the medical press, hardly knows which way to turn in the selection of the most effective antibiotic for his patient. The present purpose is not to review the choice of antibiotics for each of the infectious diseases but to emphasize the problem that exists in selecting the proper antibiotic and to discuss what the physician can do under the circumstances.

In comparison with the many antibiotics that are now available, penicillin is the most effective agent for many diseases, especially infections caused by gram-positive cocci, and it is the indicated drug for the treatment of gonorrhea and syphilis. But a most confusing aspect of penicillin therapy revolves about the question as to whether it is more advantageous to employ preparations of the antibiotic that are rapidly absorbed from the sites of administration or to use those forms that are slowly absorbed and in consequence remain in the blood for a longer period of time. It should be emphasized that the tremendous number of preparations of commercial penicillin now available have essentially the same antibacterial activity but differ primarily in their rates of absorption. The physician will make no mistake in treating those infections for which penicillin is indicated by using the inexpensive crystalline penicillin G dissolved in water, provided enough material is injected. Under no circumstances is it necessary to administer penicillin intramuscularly more frequently than every four to six hours. Infections due to those bacteria highly sensitive to penicillin, such as pneumococci and group A hemolytic streptococci, can be treated with injections given intramuscularly every 12 hours. Aqueous solutions of penicillin G in large doses are preferred for the therapy of subacute bacterial endocarditis and for staphylococcic sepsis. On the other hand, when penicillin is used for

prophylactic purposes, and in the treatment of those diseases in which a low concentration of penicillin is sufficient for the disposal of sensitive bacteria, there are advantages in using preparations of so-called depot penicillins. The physician need inject such a preparation only once every 24 hours, and, in some instances, every 48 to 72 hours. Crystalline penicillin G may be administered intermittently by the intravenous route, and under some circumstances this procedure has certain advantages, such as in the treatment of subacute bacterial endocarditis, lung abscess, and pneumococcic meningitis. The usual practice is to augment the standardized intramuscular doses with injections given intravenously.

Streptomycin and dihydrostreptomycin have essentially the same antibacterial activity. While either drug is effective in the treatment of tuberculosis, streptomycin is used more frequently than dihydrostreptomycin. Either drug is the agent of first choice for the therapy of tularemia. Streptomycin can be used in combination with other antibiotics and with the sulfonamides, as will be pointed out shortly.

In the practice of medicine it is often impossible to acquire precise laboratory information that will define the etiological agent responsible for an infection. Under these uncertain circumstances, the physician can turn to the broad spectrum antibiotics that affect gram-positive and gram-negative bacteria, as well as the rickettsiae, and even some of the larger viruses. These antibiotics have an added virtue in that they can be administered orally. With either aureomycin or oxytetracycline, many diseases can be adequately treated by prescribing a total daily dose of only 1 gm., 250 mg. being given every six hours. Because chloramphenicol does cause aplastic anemia, I have reserved this drug for the treatment of typhoid and infections not favorably influenced by aureomycin or oxytetracycline. Except for local purposes, bacitracin has been cautiously used systemically only in those cases of staphylococcic sepsis where normal renal function is present. This also applies to polymyxin B, which is the drug of choice for serious infection due to Pseudomonas aeruginosa (pyocyaneus). As already noted, neomycin is being used in these clinics orally, and preliminary observations indicate that a total daily dose of 750 mg. may be administered parenterally without toxic manifestations. Erythromycin and carbomycin have a more restricted antibacterial activity than aureomycin or oxytetracycline, but these drugs have been found useful for infections due to gram-positive cocci.

An aspect of antibiotic therapy that has occasioned considerable misunderstanding relates to the simultaneous use of two or more antibiotics. It has been demonstrated in the laboratory that the killing effect of two antibiotics for bacteria may be less efficient than if the more active of the two drugs were selected and used alone. This is an expression of antagonism.[4] There is no question that under certain restricted experimental conditions antibiotic antagonism may be exhibited, but in actual clinical practice it is highly doubtful that significant antagonism occurs. A possible exception to this conclusion relates to the simultaneous treatment of pneumococcic meningitis with penicillin and aureomycin.[5] It would appear that better results could be obtained in the treatment of this disease when penicillin was used alone. While the clinician, in the light of present knowledge, need not concern himself too much with the problem of antagonism of antibiotics in the human body, there are definite advantages in administering two antibiotics under certain conditions. There are two sensible indications for the utilization of combinations of antibiotics. First, clear-cut laboratory and clinical data are now available in which it has been demonstrated that two antibiotics will exhibit a synergistic effect against a given species of bacteria. This means that the killing action of the agents is greater than that obtained by adding together the independent effects of each antibiotic. This has been demonstrated in the treatment of subacute bacterial endocarditis with penicillin and streptomycin, in cases of staphylococcic sepsis in which penicillin and bacitracin have been used, and in some cases of brucellosis in which aureomycin has been administered along with streptomycin; however, such indisputable examples of synergism are the exception rather than the rule. Tuberculosis has been treated effectively with a combination of streptomycin and *p*-aminosalicylic acid or isoniazid, although the latter two drugs cannot properly be considered antibiotics. A second general indication for the use of combinations of antibiotics arises out of desperate clinical conditions in which an undefined mixed type of bacterial infection exists. These conditions include the rupture of a hollow viscus such as a perforated peptic ulcer, or the perforation of an appendix, where the bacterial flora of the intestinal tract may find its way into the peritoneal cavity. Under such circumstances I have not been sanguine enough to rely on a single suppressive agent like aureomycin or oxytetracycline but have administered penicillin and streptomycin empirically, and at times, along with aureomycin, in an attempt to keep the infection localized and the blood stream sterile. In an empirical fashion also, combinations of antibiotics have been tried in chronic infections of the urinary tract with variable results. It is apparent that present knowledge affords but limited indications for the use of combinations of antibiotics in the treatment of systemic infections. Optimum therapeutic results can be achieved in the majority of infectious processes by selecting the most active single antibiotic. The widespread practice of employing two, three, and even four antibiotics at the same time is inexcusable in most instances.

ANTIBIOTICS IN THE MANAGEMENT OF INFECTIONS OF THE URINARY TRACT

A perplexing therapeutic problem frequently confronting physicians concerns the use of the antibiotics in infections of the urinary tract. Although brilliant results often occur in the therapy of acute cases, the more chronic infections do not yield so readily. Because chronic disease is oftener associated with therapeutic failures, it is well to refer to the factors contributing to the deficiencies of the antibiotics under these conditions. As noted in the table, one of the commonest causes of

4. Jawetz, E., and Gunnison, J. B.: An Experimental Basis of Combined Antibiotic Action, report of the Council on Pharmacy and Chemistry, J. A. M. A. **150**: 693 (Oct. 18) 1952.

5. Lepper, M. H., and Dowling, H. F.: Treatment of Pneumococcic Meningitis with Penicillin Compared with Penicillin Plus Aureomycin: Studies Including Observations on an Apparent Antagonism Between Penicillin and Aureomycin, A. M. A. Arch. Int. Med. **88**: 489 (Oct.) 1951.

failure, even though the proper antibiotic is selected, is obstruction along the urinary tract, which impedes the free flow of urine. Unless the obstructing process is removed, favorable results with antibiotics will not be achieved, and relapses will frequently occur. Unrecognized tuberculosis of the genitourinary tract will not respond satisfactorily. Not infrequently, more than one species of micro-organism has invaded the tissues, and the selected antibiotic may be inactive against one of them. Finally, micro-organisms resistant to the administered antibiotics may be the cause of chronic disease. The species of micro-organisms that oftenest cause infections of the urinary tract include the following: Escherichia coli, Aerobactor aerogenes, Pseudomonas aeruginosa, Proteus vulgaris, Streptococcus faecalis, Micrococcus pyogenes, Klebsiella pneumoniae, and paracolon bacillus. It will be noted that most of the species involve gram-negative organisms found in the feces. Except in cases of infections due to M. pyogenes and infections caused by Str. faecalis, it becomes obvious why penicillin is not the best agent for the treatment of urinary tract infections. In fact, better results are often achieved with one of the sulfonamide preparations. In general, I have had the most favorable therapeutic results in infections due to coliform organisms when I used aureomycin. Experience with oxytetracycline has been limited. The two species of micro-organisms that are difficult to eradicate from the urinary tract are Ps. aeruginosa and P. vulgaris. The former species has been found to be highly resistant to most of the commonly used antibiotics. If normal renal function is present, polymyxin B may be tried in an effort to eliminate the organisms. Another possibility for Pseudomonas organisms involves the use of streptomycin along with sulfadiazine. Organisms belonging to the Proteus group have often been found sensitive in vitro to penicillin and chloramphenicol. Either or both of these drugs administered simultaneously have been successfully used in eliminating this species.

Factors Contributing to the Failure of Antibiotics and to Chronicity in Infections of the Urinary Tract

- Impediments of free flow of urine
  - Obstruction at bladder neck
  - Pregnancy
  - Hydronephrosis
  - Calculi
  - Malignant lesions
- Tuberculosis
- Presence of infection due to two or more species of micro-organisms
- Presence of micro-organisms resistant to antibiotics

A disturbing feature of urinary tract infections is that the disease is not infrequently caused by more than one species of bacteria. Therapy may be aimed at one species with apparent success, only to have a relapse occur, but a second species of organisms may then be apparent in the cultures. For this reason, combinations of antibiotics may have to be employed.

BACTEREMIA DUE TO GRAM-NEGATIVE BACILLI

A problem closely related to urinary tract infections is the invasion of the blood stream by coliform organisms. This type of bacteremia is occurring with increasing frequency, judging by the number of cases clinicians are seeing, and this rising incidence may be due in part to the selective action of the antibiotics in which the growth of the more sensitive bacterial species is subdued, thus permitting the multiplication of the less sensitive gram-negative organisms.[6] Waisbren[7] was able to collect within one year 29 cases of bacteremia due to gram-negative bacilli other than Salmonella at the Minneapolis General Hospital. He called attention to two forms of clinical courses exhibited by patients having this type of bacteremia. The first group included patients who were febrile but alert. In such cases the pulse was bounding, but the blood pressure was normal. The second group demonstrated a picture of shock with high fever, but the skin was clammy, the pulse thready, and the blood pressure very low. These clinical manifestations were associated with bacteremia due to Escherichia coli, Aerobactor aerogenes, or Proteus organisms. He had one case of shock due to paracolon bacilli. Borden and Hall[8] have also described this syndrome of shock and death as a result of bacteremia due to paracolon organisms. It is of interest that Waisbren did not uniformly observe shock in patients having a bacteremia due to Pseudomonas aeruginosa. The most frequent portal of entry in his cases was the genitourinary tract, and the commonest precipitating factors were catheterization and instrumentation of the urinary bladder.

The treatment of patients with bacteremia due to gram-negative bacilli poses several problems. Since most of the cases involve patients of advanced age, prompt supportive measures should be instituted along with antibiotic therapy. In initiating treatment, I select a broad spectrum antibiotic, such as aureomycin, and administer the drug in an intravenous infusion. From 250 to 500 mg. of aureomycin is given in 200 ml. of sodium chloride solution every 8 to 12 hours. In the meantime, cultures of blood are kept under observation and sensitivity tests with the various antibiotics are undertaken as soon as isolations have been made. If the patient is in a state of shock, immediate efforts should be made to elevate the blood pressure, which can be done with *l*-arterenol.[9] The failure of a patient to respond satisfactorily several hours after the first dose of aureomycin may suggest the presence of a bacteremia due to Proteus organisms, and large doses of penicillin along with chloramphenicol should be administered. In desperate cases, penicillin, aureomycin, and chloramphenicol have been used until the causative organism has been identified.

The seriousness of this form of bacteremia may be judged from the experience at the University of Minne-

6. McCurdy, R. S., and Neter, E.: Effects of Penicillin and Broad-Spectrum Antibiotics on Emergence of Gram-Negative Bacillary Flora in Upper Respiratory Tract of Infants, Pediatrics **9**: 572, 1952. Yow, E. M.: Development of Proteus and Pseudomonas Infections During Antibiotic Therapy, J. A. M. A. **149**: 1184 (July 26) 1952.

7. Waisbren, B. A.: Bacteremia Due to Gram-Negative Bacilli Other Than the Salmonella: A Clinical and Therapeutic Study, A. M. A. Arch. Int. Med. **88**: 467 (Oct.) 1951.

8. Borden, C. W., and Hall, W. H.: Fatal Transfusion Reactions from Massive Bacterial Contamination of Blood, New England J. Med. **245**: 760, 1951.

9. Wise, R. I.; Shaffer, J. M., and Spink, W. W.: The Syndrome of Vascular Collapse Due to Gram-Negative Bacteria: Its Management with 1-Norepinephrine and Antibiotics, abstracted, J. Lab. & Clin. Med. **40**: 961, 1952.

sota Hospitals. From March, 1951, to July, 1952, observations were made on 53 patients from whose blood gram-negative bacilli were isolated. Eight of these patients exhibited shock, the bacteremia being due to A. aerogenes in three, Esch. coli in two, paracolon bacilli in one, and Salmonella typhimurium in one. Although these patients received *l*-arterenol and antibiotics, six of the eight died.

STAPHYLOCOCCIC SEPSIS

When penicillin was first introduced for clinical trials, it was soon established that this agent would resolve many therapeutic problems relating to the management of staphylococcic sepsis. A decade has now elapsed in which penicillin and other antibiotics have been thoroughly evaluated in patients with staphylococcic infections. An initial feeling of optimism over what had been accomplished has been succeeded by waves of increasing pessimism. Early investigations indicated that the vast majority of strains of staphylococci isolated from human sources were sensitive to penicillin. This in vitro sensitivity was reflected in excellent therapeutic results with the drug in patients. But with the passage of time, more and more patients were encountered who were suffering from staphylococcic infections in which the offending organism was highly resistant to penicillin. In various parts of the world, there was every indication that the widespread use of penicillin had resulted in the appearance of highly resistant strains of staphylococci. This state of affairs has been demonstrated in this clinic at present, where over 50% of the strains of staphylococci isolated from human sources are highly resistant to penicillin. In other words, if penicillin were to be used in patients with staphylococcic sepsis, there would be less than a 50-50 chance of the drug being effective. When other antibiotics became available for staphylococcic diseases, the story of penicillin resistance was repeated. Strains highly resistant to streptomycin soon appeared with the increasing frequency. Resistance to aureomycin and oxytetracycline is now such a common phenomenon that approximately 40% of the strains isolated at the University Hospitals are resistant to these agents. The introduction of erythromycin appeared to resolve the problem of antibiotic resistance temporarily, but recent evidence indicates that erythromycin-resistant strains of staphylococci have appeared as a result of therapy with that agent.[10] The seriousness of the problem of staphylococcic sepsis was emphasized for the staff during the last week in 1952, when seven patients with staphylococcic septicemia were encountered on the teaching services of two hospitals, and four of these patients had acute staphylococcic endocarditis.

While there is no entirely satisfactory answer, at present, to the therapy of patients with staphylococcic infections, much can be accomplished with the antibiotics when the clinician is guided by in vitro sensitivity studies. The strain of Staphylococcus responsible for the infection should be isolated as soon as possible and subjected to the in vitro action of the different antibiotics. When the organisms are sensitive, penicillin is still the antibiotic of choice in the treatment of staphylococcic infections. If the serious nature of acute staphylococcic endocarditis is considered, it is remarkable that approximately half of the patients have been reported as recovering following the use of penicillin.[11] Even in the case of penicillin sensitive staphylococci, large doses of the antibiotic should be used, and treatment continued for many days, and even weeks, after apparent recovery. A frequent mistake is to discontinue therapy too soon. Crystalline penicillin G in water can be administered intramuscularly every four to six hours in a dose of 500,000 units. In addition, "booster doses" should be administered intravenously in doses of 1 million units in 10 ml. of sodium chloride solution every 12 hours. These latter doses should be continued until the disease is well under control, and then the dose of penicillin should be gradually reduced. In the cases of severe staphylococcic sepsis with bacteremia, and particularly in those patients having endocarditis, bacitracin has been given simultaneously with penicillin, providing the strain was sensitive to bacitracin and normal renal function was present. Since bacitracin is nephrotoxic, minimal doses have been used in the range of 20,000 units administered intramuscularly every six hours. The combination of bacitracin and penicillin need only be used in the initial week or two, after which the bacitracin should be discontinued. If the strain of Staphylococcus proves to be highly resistant to penicillin, it is necessary to turn to other antibiotics. Some patients have responded satisfactorily to either aureomycin or oxytetracycline, where the organisms have been sensitive to these drugs. I have used aureomycin intravenously in a dose of 300 to 500 mg. given intravenously in 200 ml. of sodium chloride solution every 8 to 12 hours. If improvement occurs, the drug is then administered orally alone in a dose of 0.5 gm. every six hours. I do not encourage the use of aureomycin or oxytetracycline along with penicillin. More recently, erythromycin has been employed in the clinic for the treatment of infections due to penicillin-resistant staphylococci, and, while the early results have been encouraging, I anticipate the emergence of erythromycin-resistant strains. The drug has been administered orally in a dose of 200 to 300 mg. every six hours. A combination that has been tried recently in two patients with favorable results suggests that further trials should be made and involves the use of 20,000 units of bacitracin given intramuscularly every six hours and 300 mg. of erythromycin administered orally every six hours. In severe cases of sepsis, this combination has been given for two to three weeks, and then erythromycin continued alone for another week or two. Preliminary investigations with carbomycin indicate that it is also of value in the treatment of staphylococcic infections, and should be administered in a similar manner.

COMMENT AND CONCLUSIONS

The rapid and extraordinary achievements in the treatment of infectious diseases constitute one of the outstanding advancements of modern medicine. This field of inquiry is not static, and investigations are continuing in the search for agents that will yield optimum results with the least harmful effects for the patients, and for

10. Haight, T. H., and Finland, M.: Resistance of Bacteria to Erythromycin, Proc. Soc. Exper. Biol. & Med. **81**: 183, 1952.

11. Dowling, H. F.; Lepper, M. H.; Caldwell, E. R., and Spies, H. W.: Staphylococcic Endocarditis: An Analysis of 25 Cases Treated with Antibiotics, Together with a Review of the Recent Literature, Medicine **31**: 155, 1952.

successful therapy of diseases due to viruses and fungi. It is difficult for the busy practitioner and for a hospital staff to keep up with the more recent developments. In order to crystallize the available information for practical purposes, it is suggested that each hospital staff, and especially the larger general hospitals, have a standing committee on chemotherapy, for the purpose of evaluating and recommending standard procedures for the use of the antibiotics. The various services and specialties should be represented, including the hospital pharmacy. In the teaching centers, a member of the department of pharmacology would be a valuable addition. Such a committee could periodically survey the recent developments; take inventory of problems that have arisen in their own hospital; and indicate the drugs, schedules of doses, and methods of administration for the various clinical conditions. With the increasing cost of medical care, the committee could also aid the pharmacist and the purchasing department in selecting those therapeutic agents that are less expensive and at the same time just as effective as the more costly antibiotic preparations.

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CRANIOCEREBRAL INJURIES

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This era of mechanization, with emphasis on high speed transportation, has increased the incidence of injuries to the head and all other human tissues. Therefore, in addition to a neurological examination, a careful, complete, general examination is imperative before the proper course of any treatment can be planned and instituted. All injuries must be treated in order of importance before definitive treatment of the craniocerebral injury is embarked on. Active hemorrhages must be arrested, shock eliminated, and obstructed respiratory pathways cleared. If simple oropharyngeal suction is inadequate, a tracheotomy will be necessary. The different pathological lesions resulting from craniocerebral injuries and their respective treatment can be conveniently discussed by consideration successively of the tissues from the scalp to the ventricles.

INJURIES TO THE SCALP

Traumatic lesions of the scalp may be minor, and the contusions and abrasions may require nothing more than thorough, gentle lavage with soap and water and application of nonadhering dressing of penicillin ointment or the like. Major scalp lacerations or avulsions usually require débridement, hemostasis, suturing, or some plastic procedures. To cover a small scalp loss resulting from an avulsion, the surgeon, after properly shaving, cleansing, and débriding, may simply undermine subgaleally the surrounding scalp in a radial fashion until the scalp will stretch without much tension, cover the scalp defect, and allow wound edges to be approximated with sutures.

Sometimes a large area of scalp is lost and one or two pedicle scalp flaps may have to be mobilized and swung into position to cover the denuded area. In so doing the surgeon must remember the blood supply and locate the flap's pedicle so that the arterial blood supply to the flap is maintained. If the bone is bared of pericranium, the swinging of pedicle flaps should be delayed until there is present a bed of granulation tissue with good, active circulation. Such a bed of granulation tissue can be encouraged to grow if multiple drill perforations are made through the outer table of the skull. When the granulations springing from the perforations in the outer table become confluent, a full thickness pedicle scalp flap or small free partial thickness skin grafts or a combination of both may be swung or laid in place.

Read at the Sixth Clinical Session of the American Medical Association, Denver, Dec. 4, 1952.

BONE AND DURA INJURIES

A skull fracture should in part indicate the amplitude of the forces that acted to cause the head injury. The fracture per se is not necessarily serious unless there is a depression of the skull over an essential area of cortex like the motor convolution or visual area, or the depression causes impingement on a cranial nerve as it makes its exit through a skull foramen. Skull depressions and foraminal impingement should be removed as soon as practical. Delay may cause irreversible changes and permanent disability. When the depressed bone fragments have been removed, an intradural inspection of the brain should be made. If hemorrhagic, necrotic brain tissue is present, that should be removed and the dura closed. In closed, clean wounds in children, some bone fragments should be placed in the area of decompression where they will act as osteogenic foci and promote skull reformation, which is sometimes complete and cosmetically satisfactory. Similarly treated small skull defects in adults may become solid enough to prevent pulsations and also produce a satisfactory psychological and cosmetic result. In cases with compounded skull fractures, the surgeon risks promoting infection if he replaces the bone fragments, even with liberal use of chemotherapeutic and antibiotic agents. It is safer to use tantalum or other materials for cranioplasty months after the healing of compound skull fractures.

A fracture in the region of the paranasal sinuses or thru the petrous pyramid may be associated with a tear in the dura and arachnoid, thus allowing cerebral spinal fluid to escape into the nasal cavity or auditory canals. Through such fractures and dural tears micro-organisms may enter the cranial cavity, causing meningitis and brain abscesses. Since meningeal tears over the paranasal sinuses are potentially serious, they should be "patched" intracranially as soon as the patient's condition permits. Through a transfrontal craniotomy the dural tear can be exposed and easily covered with a piece of epicranium, which can be obtained from along side the operative scalp incision. Fascia lata from the thigh is thicker, stiffer, and more difficult to bring into water-tight juxta-

position over the irregular surface of the base of the anterior fossa than is the thin, more flexible pericranium. Scarifying the dura on which the patch is to be laid promotes adherence and revitalization of a free graft.

Dural tears over the petrous pyramid with cerebrospinal fluid leakage into the external or internal auditory meatus usually can be treated satisfactorily without surgery by having the patient lie on the affected side with the head elevated. In such a position the brain acts as a tampon and soon fibrous tissue closes the dura tear. All attendants should be warned to keep applicators and other cleansing devices out of the draining ear, and a dressing fixed over the ear with adhesive tape and marked "keep out" will be helpful in this respect. Patients with cerebral spinal fluid otorrhea or rhinorrhea should be given therapeutic doses of sulfadiazine and sulfamerazine because these sulfonamide compounds are secreted into spinal fluid in concentrations approximately one-half those in blood. For adults, a dose of 1 gm. of mixture should be given every three to six hours with a similar amount of sodium bicarbonate, starting immediately after the accident. Fluids should be administered in amounts short of promoting cerebral edema yet causing excretion of 1,200 to 1,500 cc. of urine every 24 hours, a quantity that will usually prevent sulfonamide crystaluria or anuria. In addition to the sulfonamide drugs, aureomycin, 250 to 500 mg. every three to four hours, should be given because this particular antibiotic is also secreted into cerebral spinal fluid.

BRAIN, DURA, AND DURAL BLOOD VESSELS

When the dura is lacerated by a depressed fragment of skull, the underlying brain and its blood vessels are usually lacerated, too. By suction the hemorrhagic, devitalized brain tissue should be carefully removed and all bleeding controlled. If there has been a loss of dura, a free pericranial graft is taken and sutured in place, and if there has been only a dural laceration over the convexity of the brain, dural suturing will suffice. The other layers of tissues in the wound then can be treated appropriately.

Occasionally the dura subjacent to a fracture will not be lacerated but one of the dural arteries will be lacerated and an extradural hematoma forms. In such cases the patient usually suffers a head injury severe enough to become unconscious for a short period. When the patient recovers consciousness, he complains of headache and he has nausea and vomits. Usually within a matter of a few hours his condition deteriorates and he becomes progressively more lethargic, stuporous, and finally comatose. He may have a dilated pupil on the side of the extradural clot and often he will have a contralateral spastic weakness of extremities and increased tendon reflexes along with stiffness of the neck. The systolic blood pressure usually increases and the pulse and respiratory rates decrease. The lumbar spinal fluid is usually clear but the pressure is markedly elevated. Such a sequence of symptoms and signs should arouse the physician to make the diagnosis of supratentorial extradural hematoma and excite him immediately to have the clot removed surgically and to have the bleeding controlled.

Recently Schneider and Kahn [1] have emphasized the entity of extradural, infratentorial hematomas, which are easily overlooked because of low incidence of 0.5% of all extradural hemorrhages. A history of an injury to the occipital area with a fracture in this area and clinical signs referrable to the neurological structures of that location, i. e., nystagmus, hyporeflexia, ataxia, and cerebellar fits, with cranial nerve dysfunction are reasons for considering the possibility of extradural infratentorial hematoma. Clear spinal fluid under increased pressure and progressively deepening stupor makes the diagnosis more certain. The treatment is like that of supratentorial extradural hematoma, namely, the surgical removal of the clot and arrest of hemorrhage. Since an associated supratentorial hematoma may be present, a trephine exploration should also be made superior to the lateral sinus and any hematoma there also removed.

CEREBRAL VEINS

Some patients, who are usually past 50 years of age, have head injuries and apparently suffer only a cerebral concussion or mild contusion with a short period of unconsciousness or have no period of unconsciousness but do have headache with or without nausea, dizziness, and other nervous symptoms for a short period. To all appearances, the patients recover and return to work but in a few weeks or even in three or more months they have a recurrence of headache, loss of interest in work and in their own personal appearance, clouding of sensorium, increasing somnolence, and occasionally urinary incontinence. These patients often have dilation of one pupil and maybe some other cerebral localizing signs. More frequently than not, they have xanthochromic spinal fluid with increased pressure and increased total protein. Usually x-ray examination of the skull reveals no skull fractures but the pineal body, if calcified, may be seen to be displaced from the normal midline position. Patients with such a sequence of symptoms and signs following head injury, regardless of how trivial, should have bilateral trephine explorations of the skull for subdural hematomas. Since about 50% of these subdural hematomas are bilateral, they should always be trephined bilaterally. Although skulls can be trephined any place, the optimum locations for the trephinations are in the coronal suture about 5 cm. on each side of the sagittal suture. Another trephination in the temporal area on the involved side or sides makes for easy drainage. With a no. 14 or 16 French urethral catheter, all subdural adhesions can and should be broken to evacuate all loculations of blood. Drains should be left in the subdural space or spaces where hematomas have been evacuated. Rarely in an adult will the surgeon have to turn an osteoplastic flap to remove the hematoma. In infants, however, it is essential to turn a large flap and remove the neomembrane in order to prevent re-formation of hematoma or hygroma. If the trephination is done under local anesthetic on a stuporous patient, the patient may arouse during closure of the wounds and ask relevant questions. An interesting example was a stuporous obstetrician and gynecologist suffering from a large

1. Schneider, R. C.; Kahn, E. A., and Crosby, E. C.: Extradural Hematoma of Posterior Fossa, Neurology **1**: 386, 1951.

subdural hematoma who aroused after drainage of the hematoma, and during closure of wounds called out from under the operative drape, "Use some K-Y [a lubricating jelly] on those needles."

Trauma is no doubt the greatest factor in production of subdural hematoma, even though some patients having subdural hematoma do not preoperatively recall having had head injuries. Postoperatively, when the sensorium has cleared, some of these patients will recall pertinent injuries such as arising under an open cupboard door and striking the head and having inconsequential headache of short duration. The injury was thought trivial and forgotten. Because the bleeding is venous in origin, only a small clot forms to produce the first symptoms. After passage of weeks or months the subdural hematoma becomes quite large and produces symptoms and signs indicating the gravity of the patient's condition. Subdural hematomas are common in alcoholic patients who have high threshholds to pain and high indexes of forgetfulness and euphoria. Bleeding intracranial aneurysms may be associated with a complicating subdural hematoma without associated head injury.

CEREBRUM AND VENTRICLES

Rarely there may occur an intracerebral hematoma or an intraventricular hematoma that results from tearing of the intracerebral and intraventricular vessels. When these occur, they are like subdural hematomas in that they produce symptoms and signs only after a latent period. They are usually misdiagnosed as brain tumors and are treated surgically. Postoperatively in retrospect these patients may recall a head injury. Contusions to the cerebrum are common traumatic lesions but only rarely are subtemporal decompressions necessary to save a life.

GENERAL PRINCIPLES IN TREATMENT OF HEAD INJURIES

A patient who receives a head injury may at the time of first examination have no signs of intracranial hematoma formation or intracranial pressure, so it is imperative that frequent neurological examinations be made and that the vital statistics be recorded graphically at frequent intervals, for example, every one-quarter hour until the patient reacts, then every hour until stabilized, and finally every three hours until it is safe to discontinue. A record of mental status should also be made every one-quarter hour until the patient reacts and then every hour or so, as the condition requires. For temperatures of 102 F rectally or above from 10 to 15 grains (0.6 to 1 gm.) of acetylsalicylic acid should be given orally or per gavage every three to six hours. A minimum of bed covering or clothing is advisable. For higher temperatures the nurses should sponge the patient with a cool, moist cloth or cover with cold towels. An electric fan directed not at the patient but close to the patient should be helpful in decreasing the temperature.

Oxygen Administration and Position. — All patients with serious head injuries who are unconscious should receive moistened oxygen administered through a soft nasal catheter at 3 to 5 liters per minute. The head of the bed should be elevated 45 degrees when the patient's cough and gag reflexes return and when the blood pressure, pulse, and respiration rate permit. The patient should be turned every one to three hours. When the bed is level, nurses may turn the patient on the abdomen if there are no contraindications.

Pain.—For pain and restlessness ½ to 1 grain (30 to 60 mg.) of codeine can be given hypodermically as necessary every two to four hours, or acetylsalicylic acid with or without ¼ to ½ grain of codeine orally. If the patient is irrational and pain is not controlled with codeine, 2 to 4 drachms (8 to 15 cc.) of paraldehyde in iced orange juice or other agent can be given orally or rectally, mixed with an equal amount of mineral or vegetable oil, every three hours as necessary. Morphine, which depresses respiration, as does intracranial pressure, should be avoided. Barbiturates should not be used, because they normally make the patient lethargic, as does increasing intracranial pressure. By avoiding these drugs, the observer gets a true clinical picture of the patient's condition without having to discount the influence of the drugs.

Bacteriostatic Agents. — Antibiotics should be used prophylactically as indicated. Aureomycin is excreted into the cerebrospinal fluid and affects many gram-positive and gram-negative species of micro-organisms. If patients can not take aureomycin, another suitable antibiotic should be given. In cases in which meningitis complicates the injury, cultures should be made from spinal fluid and sensitivity tests made, and only those antibiotics should be used to which the organisms are most sensitive.

The sulfonamide drugs administered together are synergists. In central nervous system infections, a most effective combination is that of sulfadiazine and sulfamerazine, which are secreted into the cerebrospinal fluid in about one-half of their blood concentration. If the bacteria are not sensitive to sulfadiazine or sulfamerazine, however, they should not be used because of the risk of kidney complications. The optimum dose for adults is 1 gm. (0.5 gm. each) of sulfadiazine and sulfamerazine given with 1 to 2 gm. of sodium bicarbonate every three to eight hours, depending on the size of the patient and the severity of the infection.

Fluids.—Fluid intake should be limited to 1,500 cc. for the first 24 hours or maybe longer, unless the temperature is 102 F or above or unless sulfonamides are used and then the intake should be increased as indicated in order to obtain a urinary output of 1,500 cc. per 24 hours. Fluids may be given by vein, but, if the patient is unconscious, the fluid and diet, as a formula, may be given by gavage tube. In cases in which intracranial pressure is increased owing to cerebral edema associated with cerebral contusion, it is important to limit fluid intake and not give the sodium ion, to dehydrate by giving a saline cathartic (such as magnesium sulfate, sodium phosphate, or citrate of magnesia) every morning, to do spinal punctures, and to reduce pressure by one-half of the increased pressure (by one-half what the pressure is over the normal of 15 cm. of water pressure).

Administration of hypertonic intravenous solutions probably is indicated in only a few cases of cerebral edema. The most valuable hypertonic solution is human serum albumin, which should be given in 60 to 80 cc. amounts in not less than 10 minute periods, every 8 to 10 hours. It should be repeated as often as indicated. Lastly, in addition to the foregoing measures to reduce cerebral edema causing increased intracranial pressure,

extensive bilateral subtemporal decompressions may be in order, with removal of as much fluid from the subarachnoidal and subdural space as possible.

Food.—If the patient is conscious, he should be given a liquid to regular diet as tolerated. If he is unconscious, he should be given by gavage a formula, made up to 1,500 cc. containing 1,500 calories, composed of whole milk, whole eggs, and molasses; 375 cc. are given every six hours. The volume, the caloric content, and the frequency of administration may be varied to suit individual cases, and some all-inclusive vitamin preparation should be added. Medicaments for oral administration may be given in solution or be crushed and put into solution to be given through the gavage tube.

Antiserums and Antitoxin. — Polyvalent antiserums should be given in all cases of contaminated wounds of the head, and tetanus antitoxin in cases of perforating or puncture wounds if the patient has not been protected with toxoid. If the patient has previously had toxoid, a booster dose may be all that is indicated.

Ambulation. — Patients suffering from cerebral concussions should be ambulated as soon as they recover consciousness and stability. Those with severer injuries such as cerebral contusions with and without subarachnoid hemorrhages should be allowed to sit on the edge of the bed and dangle their feet about 24 hours after active hemorrhage has ceased. The amount of blood found in successive lumbar spinal taps should reveal when the active hemorrhage stopped. The initial activity should not be strenuous but should be limited to a few minutes of walking to the bathroom or the like. Subsequently the patient should rest and later be ambulated until he is able to remain out of bed and be active all the time. It is extremely important to examine the patient repeatedly for signs indicative of cerebral localization or increasing intracranial pressure, both of which might indicate hematoma formation. When the patient has recovered sufficiently, he should return to his job, at first maybe only for part time, but nonetheless working and making a part of his living. Patients with cerebral lacerations that required débridement may not be rehabilitated so rapidly; however, as soon as possible they should be allowed to dangle their legs, to get into a chair, to walk, and to work, and should be encouraged to engage in normal activities as much as possible.

Spinal Fluid Examinations.—Not all patients suffering from head injuries need spinal fluid examinations. Lumbar puncture with pressure determination is indicated when the patients' vital signs and mental status suggest increasing intracranial pressure, which is usually manifested by progressively rising blood pressure, and by progressively slowing pulse and respirations. Such a patient usually becomes progressively more drowsy and finally stuporous and comatose; however, when the pulse is very rapid, respirations are very fast and shallow, and the blood pressure is low, such radical changes in vital signs are usually signs of a very serious circulatory and respiratory collapse and impending death. If in addition to changes of vital signs, there are cerebral localizing signs and the spinal fluid is clear and under increased pressure, it is almost certain to mean the patient has an extradural hematoma and needs immediate surgery. On the other hand, if the patient has bloody spinal fluid under increased pressure, the examiner must be able to evaluate whether or not this is only a cerebral contusion with cerebral edema and whether or not surgical decompression is required. Patients with traumatic subarachnoidal hemorrhage usually have restlessness, headache, nausea and vomiting, photophobia, and a stiff neck but no cerebral localizing signs and no alteration in vital statistics. The spinal fluid in addition to being bloody will usually be under increased pressure. Daily or semidaily lumbar spinal drainage may be indicated to reduce the pressure by one-half of the increased pressure and to remove fluid until it is no longer bloody.

All elderly and some younger persons who have suffered cerebral contusions or worse lesions should be benefited by administration of 3¾ grains (250 mg.) of caffeine sodium benzoate hypodermically every three hours from 6 a.m. to 9 p.m. This drug seems to make the patients more responsive, alert, and active, and helps to clear their sensoriums so they can be discharged from the hospital and returned to daily routine more quickly.

Not infrequently a patient comes to the physician saying that he had a head injury a matter of days, weeks, or even months before and that he is "worried no end" because he has had a headache more or less ever since, and the headache is getting increasingly worse and interferring with his job and at times even preventing his sleep. The headache is worse if he is tired or nervous and if he works in the hot sun. In addition he complains of nervousness, easy fatigability, and forgetfulness. Those who associate with him complain of his irritability, and intolerance to noise and to children's play. Complete neurological examination, x-ray examination of the skull, electroencephalography, spinal fluid studies, and even air studies usually reveal no space-occupying lesion or other demonstrable organic brain disease. Repeated examinations, reassurance, encouragement from the physician, and the patient's own perseverance in an interesting job will divert his thoughts of his own condition and eventually bring about relief of symptoms. Such a syndrome is commonly called a post-traumatic syndrome. It is my personal experience to have patients with arterial hypertension frequently develop the so-called post traumatic syndrome, perhaps because they are basically inclined to worry or to work very hard.

SUMMARY

Head injuries are discussed in a general way, with emphasis placed on lesions that require surgical intervention. The general principles of treatment are discussed in detail.

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Weight Reduction and Atherosclerosis.—The relationship between obesity and atherosclerosis has been studied in a large clinical experiment. Significant weight reductions in 39 patients revealed that the serum lipoproteins are significantly reduced by this procedure in those patients with initially high levels, but are not significantly altered in patients with initially low levels. The cholesterol levels are unchanged. If the hypothesis relating high serum levels of lipoproteins to the development of atherosclerosis can be confirmed, then this experiment will supply evidence indicating the beneficial effect of weight reduction.—F. J. Stare, M.D., Nutritional Research in Public Health, *Postgraduate Medicine*, April, 1953.

CHANGE IN ELECTROLYTES IN A CASE OF PARATHION POISONING

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and
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Our purpose in reporting this case of parathion poisoning is to make known (*a*) the observed changes in the serum pH and calcium, phosphorus, and potassium levels and (*b*) the hitherto unreported residual manifestations affecting the central nervous system resulting from anoxia, prolonged unconsciousness, convulsive seizures, electrolytic and pH shifts, and/or severe cholinesterase depression. These latter may serve as a warning of the potential toxic effects of the chemical in nonfatal cases. The former, it is to be hoped, will stimulate follow-up studies in order to determine whether the changes in pH and electrolyte concentration are as determinant of the variations in symptoms, the severity of poisoning, and the prognosis as are the changes in the cholinesterase levels of the plasma and cells.

REPORT OF A CASE

A 19-year-old man had worked in close contact with parathion for a total of 69 hours before onset of illness (table 1). This man mixed materials in a spray tank and then delivered them to a speed sprayer. He never went inside the tank. He was equipped at the beginning of each day's work with clean coveralls, natural rubber gloves and hat, and a respirator. He took a shower at the end of each day's work before leaving the premises. Each day, he washed his hands and face before eating the noon meal. He was instructed to wash his hands and face at each of the two break periods during the day. He had never worked with parathion prior to this time. A cholinesterase determination,[1] done four days before his admission to the hospital, showed a level of 144% in the red blood cells and 82% in the plasma. He felt well on the morning of July 20, 1952, and, on reporting to work, he changed into clean protective coveralls, rubber gloves, and a mask. He worked mixing parathion throughout the morning as usual and noticed no ill effects. The weather was excessively warm and there was little breeze. He ate well at noon but shortly thereafter began to feel ill and told his co-worker that he was dizzy. The superintendent was called immediately. He found the patient somewhat stuporous, perspiring freely, and complaining of nausea, vertigo, diminution of vision, and headache. The patient vomited shortly thereafter and was brought to the hospital emergency room at 4 p. m. the same afternoon. At that time he was unable to stand, was extremely groggy, and became comatose. His color was ashen gray, and respirations were labored. He appeared to be in rather profound shock, but his blood pressure was 154/84 mm. Hg, his pulse 180, bounding and regular. His rectal temperature was 102 F. It was thought that he was gravely ill, and artificial respiration was begun immediately. The pupils were fixed and pinpoint, and there was marked conjunctivitis. There was copious serosanguinous, frothy exudate coming from the mouth and nose, and the neck veins were markedly distended. The heart sounds were normal except for a tachycardia. Moist rales were heard in the lung fields. The abdomen was normal, and the extremities showed marked decrease in only the deep tendon reflexes bilaterally. Babinski's sign was not elicited.

Voluntary respiration had ceased on admission, and the patient did not respond to painful stimuli. He underwent repeated intermittent, generalized tonic and clonic convulsions of approximately two minutes' duration. Oxygen was first administered by mask and then continued by intratracheal tube so that the anesthetist might maintain forced respiration. In spite of therapy, voluntary respirations were not resumed until 10:30 p. m. At that time, breathing became Cheyne-Stokes in character and, later, changed to typical Kussmaul's respirations. Normal respirations became established on the morning of July 21.

The patient was given 0.04 grain (0.002 gm.) of atropine subcutaneously and 5 cc. of nikethamide (Coramine) intravenously on admission. Intravenous administration of a solution of 5% glucose in saline was also started. During the first eight hours of hospitalization, the patient received 0.18 grain (0.011 gm.) of atropine, of which 0.02 grain (0.001 gm.) was given intravenously, 20 cc. of nikethamide, 500 cc. of citrated blood, and 2,000 cc. of 5% glucose in isotonic sodium chloride solution, and 1,000 cc. of ⅙ molar sodium lactate solution intravenously. Oxygen was administered by the anesthetist during this time, and 10 grains (0.65 gm.) of phenobarbital sodium was given intramuscularly, plus 200 mg. of secobarbital (Seconal) sodium intravenously in an effort to control the convulsions that occurred periodically throughout this period. It was soon noticed that the cannister on the anesthetic machine became too hot to touch. When the cannister was replaced, the same situation developed within 20 to 30 minutes. From this, it was assumed that the excessive activity of the soda lime must reflect a marked acidity in the expired air. Therefore serum pH and other blood chemistry values were determined; the serum pH at this time was 6.76 (table 2).

On the morning of the second hospital day, respirations were normal, but the intratracheal tube was left in place and administration of oxygen was continued. The patient was still unconscious. His rectal temperature varied from 102 to 103.6 F but tended to fall during the day. The pulse rate slowed to between 100 and 110 and became less bounding. During the preceding evening, the patient had vomited several times, and an intranasal tube was inserted for gastric lavage and drainage. This tube was left in place. The secretions from the respiratory tract decreased after atropine was given but were not well controlled for a period of at least 24 hours. An electrocardiogram showed no marked changes characteristic of potassium poisoning, although the serum potassium level was elevated. Because of his convulsive seizures, the needle came out of the patient's vein on numerous occasions; it was finally replaced by a polyethylene tube to prevent further extravasation of blood and other fluids into the subcutaneous tissues. During the 24 hours of the second day, the patient received 0.12 grains (0.007 gm.) of atropine subcutaneously, 100 cc. of whole blood, 4,000 cc. of additional fluids, and 925 mg. of secobarbital sodium administered intravenously to control convulsions.

Starting shortly after admission, a combination of penicillin and dihydrostreptomycin was given twice daily in an effort to prevent severe respiratory infection. Blood chemistry studies were repeated on the morning of the second day (table 2). The serum pH and the calcium-phosphorus ratio had returned to normal. A complete blood cell count made on admission was not remarkable except for a leukocyte count of 28,150. The urine showed albumin, 2+, and sugar, 4+, but this specimen was obtained after one liter of glucose had been given intravenously. Inadvertently, the vomitus, urine, and the excretions from the respiratory tract were discarded on the initial day. After that, examination of these wastes showed no parathion, cholinesterase activity, or cholinesterase inhibitor effect. No information was obtained by analysis of the soda lime except that it had been neutralized by a considerable amount of acid.

On the morning of the third day, the pupils, which had hitherto been extremely small, began to dilate for short periods of time after atropine was given, and the cholinesterase levels began to rise satisfactorily in both blood and plasma. In the

1. Michel, H. O.: An Electrometric Method for Determination of Red Blood Cell and Plasma Cholinesterase Activity, J. Lab. & Clin. Med. 34: 1564, 1949.

course of that day, the patient had many convulsions; the duration of these convulsions increased over that of the earlier ones, which had lasted two minutes. In this 24 hour period, he received a total of 700 mg. of secobarbital sodium intravenously, 0.06 grain (0.004 gm.) of atropine, 500 cc. of whole blood, and 2,000 cc. of ⅙ molar sodium lactate. His rectal temperature reached a peak of 102 F, and he seemed generally improved.

On July 23, the convulsions ceased, but the temperature rose to 104.4 F. There were numerous liquid, involuntary stools. The urinary output by continuous catheter drainage remained conscious for 84 hours. His temperature during this day rose twice to peaks of 104 F. His pulse rate remained about 100. He cooperated to the extent of expectorating mucus and swallowing with some difficulty. He asked for fluids. He had no convulsions during this day, and his pupils remained well dilated. He received no more atropine. In the course of the day, he received 500 cc. of blood and 3,000 cc. of other fluid via the polyethylene tube. He received 1,000 mg. of oxytetracycline (Terramycin) intravenously, and administration of penicillin was continued. The cholinesterase levels had risen to 88% in the red blood cells and 61% in the plasma by 4

TABLE 1.—*Summary of Patient's Work with Parathion*

Day July, 1952	Hours Worked Directly with Parathion	Hours Worked in Coveralls Contaminated by Parathion	Material Handled, Lb.			
			Borax	Wettable Sulfur	Parathion Powder (15% Wettable)	Arsenate of Lead
10	10	..	120	1,200	400	..
11	12	..	60	600	200	54
			105	1,050	350	..
12	10	..	105	1,050	350	94½
			45	450	150	..
13	5	..	30	300	100	27
			30	300	100	..
14	3	6	30	300	100	27
	5	..	...	300	96	..
15	2	..	...	100	32	..
16	4	8	...	275	88	..
17	10	..	120	1,200	400	..
18	0	..	...	.....	...	..
19	0	..	...	.....	...	..
20	8	..	135	1,350	450	..
Total concentrated material	..	..	780	7,800	2,600	202½
Total diluted material	..	..	...	675	216	..
Grand total	69*	14	780	8,475	2,816	202½

* Of the 69 hours spent working with parathion, 58 hours were spent working with concentrated material and 11 hours were spent working with diluted material.

TABLE 2.—*Results of Laboratory Studies of Blood and Serum*

Hospital Day	1		2		3		4		5		6	7	8	9	12
Hour	4 p.m.	8 p.m.	8 a.m.	4 p.m.	8 a.m.	8 p.m.	8 a.m.	2 p.m.	8 a.m.	4 p.m.	8 a.m.	8 a.m.	8 a.m.	8 a.m.	8 a.m.
Cholinesterase level in % of normal															
Red blood cells	17	2.6	11.0	22.0	29	50	52	49	59	88	78	73	70	86	96
Plasma	14	1.4	1.4	7.1	17	39	39	42	67	61	61	65	75	76	119
Serum pH	..	6.76	7.89	..	..	..	..	..	..	..	..	..	..	..	..
Calcium															
(mg. per 100 cc.)	..	6.0	10.0	..	..	..	..	..	..	..	..	..	..	..	..
(mEq.)	..	3.0	5.0	..	..	..	..	..	..	..	..	..	..	..	..
Phosphorus															
(mg. per 100 cc.)	..	11.42	3.45	..	..	..	..	..	..	..	..	..	..	..	..
(mEq.)	..	6.6	2.0	..	..	..	..	..	..	..	..	..	..	..	..
Potassium															
(mg. per 100 cc.)	..	42.6	32.08	..	35.2	..	17.0	..	..	..	..	..	..	..	..
(mEq.)	..	10.9	8.24	..	9.04	..	4.36	..	..	..	..	..	..	..	..

* All cholinesterase determinations were calculated according to the method described by Michel.[1]

satisfactory. In the 24 hours of July 23, he received 20 grains (1.29 gm.) of phenobarbital sodium intramuscularly, 500 cc. of whole blood, and 2,000 cc. of 5% glucose in sodium chloride solution. He received only 0.04 grain (0.003 gm.) of atropine, and his pupils now were normal in size.

Total medication in this first 80 hours of hospitalization, was two-fifths or 0.4 grain (0.024 gm.) of atropine, 2,325 mg. of secobarbital sodium, 25 cc. of nikethamide, 30 grains (2 gm.) of phenobarbital sodium, 2,500 cc. of whole blood, and 12,000 cc. of other fluids administered intravenously. The patient still had not regained consciousness. There was considerable subcutaneous swelling in both arms, especially at the site of extravasation of fluids from the first day's intravenous injections in the right arm.

At 4 a. m. July 24, the fourth hospital day, the patient regained consciousness for the first time. He had been unp. m. on July 24. The swelling in both arms had decreased somewhat.

On the morning of July 25, the rectal temperature had dropped to 100.4 F, and the pulse was 84. The patient was extremely restless but showed no signs of any convulsive seizures. He was given sedatives and antibiotics, and 3,000 cc. of fluids was administered intravenously during the day. Swallowing was still difficult. Administration of oxygen by nasal catheter was continued.

On the morning of July 26, the sixth hospital day, the constant administration of oxygen was discontinued; oxygen was administered occasionally by BLB (Boothby, Lovelace, Bulbulian) mask. His temperature did not rise. Blood, 500 cc., and 2,500 cc. of fluids were given intravenously. The urinary output remained good, and the urine showed only 1+ albumin with a few red blood cells.

On July 27, one week after the patient's admission, the polyethylene tube was removed from his vein. His rectal temperature was 98.6 F, and his general condition was much improved. He received only 1,500 cc. of fluids intravenously during this day. Administration of antibiotics was continued. Roentgenographic examination of the chest on the eighth hospital day revealed an increase in the lung markings, particularly in the right base.

Throughout the remainder of his hospital stay, which lasted until Aug. 7, 1952, the patient improved rapidly. Although the cholinesterase levels returned to normal, it was obvious that the patient was confused, somewhat amnesic, and definitely child-like in his reactions and attitudes. He had a rather severe stomatitis that was felt to be due in part to the antibiotics he had been given and in part to the trauma that resulted from intranasal and intratracheal intubation. He showed a peripheral neuritis that involved the thumb and first finger of the right hand, which presumably resulted from trauma to the antecubital space during convulsions while fluids were being administered intravenously.

At the time of discharge, the urine was normal except for a trace of albumin, routine blood values were entirely normal, and cholinesterase determinations showed a plasma concentration of 119% and a red blood cell concentration of 96%. Determinations of blood sugar, chloride, proteins, sulfobromophthalein (Bromsulphalein), cephalin flocculation, and icterus index were normal a day after admission. The prothrombin time was very slightly increased.

TABLE 3.—*Cholinesterase Activity in Blood*

Age of Specimen	Cholinesterase Activity in % of Normal *	
	Red Blood Cells	Plasma
Specimen taken directly from donor	109%	133%
Specimen taken immediately after blood was drawn †	110%	133%
1 day	110%	135%
2 days	108%	130%
1 week	108%	132%
2 weeks	104%	118%
3 weeks	100%	110%

* All cholinesterase determinations were calculated according to the method described by Michel.[1]

† Specimens from blood drawn in Baxter Transfuso vac (500 cc. blood in 120 cc. dextrose-sodium citrate-citric acid solution) and refrigerated.

COMMENT

Observation of this patient suggests to us that the clinical manifestations of parathion poisoning may not be entirely the result of the anticholinesterase activity and consequent acetylcholine action per se but that the anticholinesterase activity and acetylcholine action may represent in part the result of marked changes in electrolytes and serum pH. The possibility that there might be a decrease in cholinesterase activity in blood that has been allowed to stand for some time was entertained, but the decrease was found to be negligible (table 3). We are, of course, well aware that these findings represent only a single instance of severe poisoning and that these observations are unconfirmed and consequently permit no generalization. Individual and variable responses are recognized to be caused by poisons from the anticholinesterase group of parasympathomimetic chemicals. It is also recognized that the changes observed here may be neither characteristic nor typical. It is felt that the action of this group of substances is perhaps imperfectly understood.

SUMMARY AND CONCLUSIONS

Severe, acute parathion poisoning in a 19-year-old man is reported, and the changes in electrolytes and serum pH are noted. In retrospect, we realize, because of the delayed decrease in bronchial secretion and change in size of his pupils, that the patient was given inadequate amounts of atropine during the first eight hours of hospitalization. We feel that his recovery was due in part to more adequate amounts of blood used. The relatively rapid rise in the cholinesterase activity from an extremely low level is thought to have been the result of these transfusions. The advisability of early treatment of parathion poisoning is emphasized; administration of infusions containing properly adjusted and adequate amounts of calcium and sodium bicarbonate is suggested.

Information from the patient's employers and from clinical evidence suggests that poisoning was the result of accidental or careless ingestion of a relatively large amount of the chemical. This emphasizes the importance of scrupulous adherence to safety measures and techniques.

It is not our intention to postulate any new mechanism for the symptomatology of parathion poisoning but merely to mention the possibility that mechanisms do exist in addition to those that have already received attention. We realize that a single isolated case of severe poisoning furnishes inadequate material from which to draw any general conclusions. Our observations on the electrolytic changes, especially the reversal of the calcium-phosphorus ratio and the prolonged elevation of the potassium level, seem to indicate the possibility of a somewhat different approach to an inadequately understood problem. We hope that other, more experienced investigators may, on a larger and more carefully controlled scale, elucidate or refute the importance of these isolated observations.

122 S. Kentucky Ave. (Dr. Annis).

Prognosis in Coarctation of Aorta.—Since most children and young adults with coarctation of the aorta do not have symptoms, there is a rather widespread belief that the malformation is an innocuous affair. The fact that a few humans with aortic narrowing have lived to advanced old age has given a false impression that the prognosis is generally not serious. There is now increasing evidence to show that coarctation leads to crippling complications or even fatality in a very large percentage of cases.

A study of the prognosis for humans with coarctation has indicated that about one-fourth of them have lived through a rather long life with little or no incapacitation, that about one-fourth have died of rupture of the aorta, that one-fourth have died from superimposed bacterial endarteritis, and one-fourth have died from the hypertensive state. In the last group, death occurred either from cardiac failure or from intracranial hemorrhage.

. . . The average age at death (including persons who have died from coarctation or one of its complications) has been about 30 years. It has become quite clear that, while some subjects may live a long and useful life with coarctation, the abnormality is one which generally brings great hazards to its possessor. It is this knowledge which prompts surgeons to attempt removal of aortic obstructions in the hope of bettering the outlook, particularly in alleviation of the hypertensive state.—R. E. Gross, M.D., Coarctation of the Aorta, *Circulation,* May, 1953.

PARENTERAL ADMINISTRATION OF TRYPSIN

CLINICAL EFFECT IN 538 PATIENTS

Irving Innerfield, M.D., Alfred Angrist, M.D.
and
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Intravenous administration of trypsin consistently produced fibrinolysis in recent dog and rabbit experiments.[1] This observation suggested that intravenous trypsin therapy might affect the fibrin network of human intravascular thrombi. Accordingly clinical studies were initiated, and we now report satisfactory results with trypsin in 71 of 74 patients with thrombophlebitis (63 patients receiving it intravenously and 11 intramuscularly). During treatment of these patients with trypsin it was apparent that the associated signs and symptoms of acute inflammation subsided and cleared up in two to three days, whereas lytic effects on the thrombi occurred much more slowly. This unexpected finding suggested that trypsin initiates biochemical reactions resulting in prompt and sustained subsidence of acute inflammation. Thrombolytic changes apparently occur later. It is the purpose of this paper to present clinical observations based on 6,456 trypsin infusions to 538 patients supporting the view that trypsin rapidly suppresses acute inflammation of diversified origin (bacterial, viral, allergic, and chemical).

METHODS AND MATERIALS

Under sterile conditions a vial containing 10 mg. of trypsin was dissolved in 3 cc. of isotonic sodium chloride. This solution was then added to 100 cc. of isotonic sodium chloride, and 1 cc. (10 mg.) of methapyrilene hydrochloride (Histadyl) was introduced into the flask. Since trypsin in solution loses approximately 40 to 50% of its proteolytic action in three hours, the intravenous infusion was started immediately following preparation of the solution. Each dose consisted of 10 to 15 mg. of trypsin dissolved in 100 cc. of isotonic sodium chloride solution. A typical course of therapy consisted of 10 mg. of trypsin per infusion, twice daily for five to seven consecutive days. Earlier in the investigation larger single doses, i. e., 250 mg., were used with no greater therapeutic effects being noted in the conditions under study. The rate of intravenous administration of trypsin did not exceed 30 drops per minute after it was observed that this factor was critical in producing untoward reactions. Citrated and whole blood samples were obtained prior to, at the half-way mark, and at the termination of each trypsin infusion. All prothrombin determinations were done according to the method of Quick. Fibrinogen was determined by the method of Greenberg. The Innerfield, Angrist, and Benjamin method [2] of antithrombin titer determination was utilized. Factor 5 was measured by the method of Stefanini, and the Conley, Ratnoff, and Hartmann method for fibrinolysis assay was utilized. The coagulation time determinations were done by the Lee and White method. Blood clotting viscosity studies were determined with the use of the Rich-Roth "ultra-viscoson" (an electronic instrument that uses ultrasonic waves to measure the viscosity of Newtonian liquids and the apparent viscosity of non-Newtonian liquids continuously and automatically). In addition the Coombs' test was done, as well as complete blood cell counts and differentials and albumin-globulin ratios.

The patients comprising the study were divided into two groups: (*a*) control patients, including those with arteriosclerotic heart disease (35), hypertensive vascular disease (35), hypertrophy of the prostate (15), and diabetes mellitus (25), and (*b*) patients with acute inflammation who were treated with intravenously administered trypsin (428). The control patients were elderly, chronically ill persons selected from the wards of a large municipal hospital, none of whom exhibited gross thrombotic or inflammatory manifestations. The patients who presented evidence of acute inflammation received either complete or incomplete courses of intravenously administered trypsin (see table). The anatomic distribution of thrombophlebitis included the calf, the popliteal region, and the thigh. The signs and symptoms consisted of pain, edema, redness, Homans' sign, fever, elevated sedimentation rate, leukocytosis, and inability to walk. Since in this study the acute inflammatory reaction following thrombophlebitis was not microbial in origin, antibiotics were not used during this investigation. Prior to hospitalization, several patients were treated at home with bed rest and antibiotics without effect. All patients with arthritis presented evidence of rheumatoid arthritis according to the standards of the New York Rheumatism Association as given by Steinbrocker, Tragger, and Batterman. Clinical and roentgenographic evidences of peripheral rheumatoid arthritis were obtained, and only patients having a chronic, but active, course of the disease were selected for treatment. Activity was determined by joint immobility, heat, soft tissue swelling, redness, joint effusion, pain, tenderness, fever, leukocytosis, and an elevated sedimentation rate. The patients were both men and women, with ages ranging from 19 to 64 years,

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Mr. Daniel Pitcoff gave technical assistance. Dr. Franklyn Theis Jr., Nyack, N. Y., supervised the care of six patients with retinal thrombosis.

The trypsin used in the experimental and clinical work was obtained from the Armour Laboratories (Tryptar and Enzar) and the National Drug Company (Parenzyme and Parenzyme in oil).

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Assistant Professor of Physiology (Dr. Innerfield), and Clinical Professor of Pathology (Dr. Angrist), New York Medical College; Research Associate in Pathology and Chief of the Clinical Enzymology Clinic (Dr. Innerfield), Director of Pathology (Dr. Angrist), and Associate Pathologist and Associate Hematologist (Dr. Schwarz), Jewish Memorial Hospital. Also affiliated with the Flower and Fifth Avenue Hospitals and the Metropolitan Hospital.

1. (*a*) Innerfield, I.; Schwarz, A. W., and Angrist, A. A.: The Fibrinolytic and Anticoagulant Effects of Intravenous Crystalline Trypsin, Bull. New York Acad. Med. **28**: 537-538 (Aug.) 1952; (*b*) Intravenous Trypsin: Its Anticoagulant, Fibrinolytic and Thrombolytic Effects, J. Clin. Investigation **31**: 1049-1055 (Dec.) 1952.

2. Innerfield, I.; Angrist, A., and Benjamin, J. W.: Antithrombin Titer in Acute Pancreatitis, Am. J. Med. **12**: 24-33 (Jan.) 1952.

the average being 43. The duration of the disease varied from 6 months to 20 years, with an average of 11 years. Thus, this study comprised a group of patients in whom plasma antithrombin and prothrombin inhibitor determinations were performed before and at the midway point of each trypsin infusion.

Clinical Results of Parenteral Administration of Crystalline Trypsin in 428 Patients

Diagnosis	No. of Patients	Average No. of Treatments	Average Single Dose, Mg.	Average Days of Treatment	Results
Acute rheumatoid arthritis	18	9	15	7	Rapid reduction in edema, less pain, greater range of motion, lowering of ESR in 15 patients; 3 relapses
Acute gouty arthritis	7	7	10	5	Prompt subsidence of signs of acute inflammation in 5 patients. One patient showed improvement after 5 treatments. One did not respond
Acute thrombophlebitis	74	11	10	6.5	Rapid decline in signs and symptoms of acute inflammation in 71 patients. Three cachectic patients (carcinomatous) did not respond
Thromboangiitis obliterans	8	10	10	7	Prompt relief of intermittent claudication. Each patient relapsed within 4 weeks. Symptoms again controlled under ambulatory treatment with trypsin
Coronary thrombosis	7	8	10	8	One death. Remaining 6 patients made uneventful recovery
Atypical virus pneumonia	9	10	10	6	Prompt reduction in cough, ronchi, and expectoration. General improvement within 36 hr.
Basilar artery thrombosis	3	20	10	14	Patients improved. No conclusive evidence of trypsin effect
Cerebral thrombosis	9	20	10	14	Same as above
Popliteal embolus	5	10	50	5	No improvement
Saddle embolus of aorta	2	10	50	2	No effect. Both patients died 48 hr. after seen
Massive thrombosis, varices of anterior abdominal wall	2	15	15	15	Complete disappearance of thrombi 4 weeks after termination of treatment
Diabetic carbuncle	4	10	15	15	In each instance mass was softened and ready for incision and drainage within 48 hr.
Ischemic purulent leg					
Ulcers	18	20	10	20	Good clinical response only in those cases presenting an acute inflammatory component
Diabetic gangrene of toe	19	20	10	15	
Diabetic ulcer of leg	31	20	10	15	
Postoperative thrombophlebitis	12	10	10	7	Disappearance of acute inflammatory component in 48 hr.
Post thrombophlebitis syndrome	8	15	10	15	
Chronic thrombophlebitis	4	20	10	20	Reduction of edema after 4-5 treatments
Phlebothrombosis	10	20	25	14	
Tuberculous adenitis	5	10	50	7	Disappearance of acute signs. Spontaneous rupture of abscess
Acute meningoencephalitis	3	14	10	10	Dramatic drop in temperature within 48 hr., marked clinical improvement
Influenza	7	14	10	10	
Cystic fibrosis of the pancreas	2	7	10	7	Marked thinning of bronchial secretions. One patient treated in terminal stage died. Autopsy confirmed thinning of secretions
Acute bronchitis	13	7	10	5	Drop in temperature within 48 hr.
Chronic bronchitis	7	12	10	12	Thinning of mucous secretions eased symptoms
Chronic bronchiectasis	12	15	10	25	
Scleroderma	2	20	10	20	Initial marked improvement of skin tension, relapse after 4 weeks
Boeck's sarcoid	1	20	10	20	No effect
Empyema	5	15	15	15	Drop in temperature after 48-72 hr., thinning of the exudate, easy drainage
Lung abscess	3	15	15	15	
Infected bronchopleural fistula	7	15	25	15	
Bronchial asthma	17	15	10	20	Amelioration of symptoms, thinning of mucus
Atopic dermitis	7	8	10	8	
Pustular eczema	3	8	10	8	
Acute eczematoid dermititis	5	6	10	6	Subsidence of the signs and symptoms of acute inflammation in 24-48 hr.
Herpes zoster	4	8	10	8	
Duhring's disease	2	6	10	6	
Neurodermititis	3	8	10	3	
Acute sinusitis	14	5	10	3	Subsidence of acute signs in 48 hr.
Chronic sinusitis	5	5	10	3	
Peritonsillar abscess	3	5	10	3	Softening of swelling and drop in temperature in 24-48 hr.
Thrombosis of central retinal artery	3	10	15	8	No effect
Thrombosis of central retinal vein	12	10	15	8	Subsidence of retinal edema in 24-48 hr.
Acute iridocyclitis	5	10	10	8	Dramatic improvement within 3-5 days
Glaucoma	3	10	10	10	Improvement of symptoms in 3-5 days. Recurrence occurred in each case ameliorated by follow-up treatment
Lymphogranuloma venereum	3	4	10	4	Subsidence of mass, fever, and pain
Acute gonorrheal urethritis	3	10	10	8	Subsidence of acute signs in 24-48 hr.
Proteus vulgaris infection of urinary tract	7	10	10	8	Urine cultures became sterile
Acute hemorrhagic cystitis	2	10	10	8	Recurrence in 4 cases of Proteus vulgaris infection, which cleared after repeat treatment
Infected pilonidal abscess	5	10	25	8	Subsidence of acute inflammatory signs in 48-72 hr.
Acute proctitis	2	10	10	10	
Acute ulcerative colitis	3	14	10	14	Drop in temperature in 72 hr. Reduction of bowel movements to 2 formed stools daily

extensive changes had occurred and in whom there was a pronounced degree of limitation of activity. The duration of the acute phase of the illness varied from 8 to 72 hours. In order to detect excess blood trypsin levels,

LABORATORY RESULTS

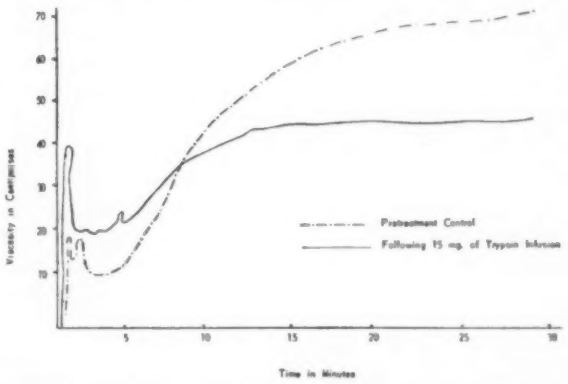
Some of the laboratory results are summarized in the table. A decrease in prothrombin to 86% of normal as determined by the Quick method, in which the normal

value is 12 to 14 seconds, was observed after the administration of 100 mg. of trypsin. Except for a moderate increase in prothrombin time, none of the factors measured showed a marked deviation from the normal level in the dose range of trypsin employed, i. e., doses up to 400 mg. With the Greenberg method, the fibrinogen levels in the controls dropped from 350 mg. to 330 mg. per 100 cc. with the 400 mg. trypsin dose. No changes whatever occurred in the fibrinogen level when trypsin was given in doses up to 350 mg. As measured by the Innerfield, Angrist, and Benjamin method, the antithrombin titer was 25 seconds after a five minute incubation period. This compared with 25 seconds at the 400 mg. trypsin dose level. Thus the antithrombin titer was not altered during the administration of the aforementioned trypsin dose. The normal level of factor 5 as measured by the Stefanini method, was 750 units. It was determined that there was a very slight but steady decrease in factor 5 with each increment in trypsin dosage; however, 705 units at the 400 mg. level compared favorably with the control level of 750 units. With the Conley, Ratnoff, and Hartmann method, fibrinolysis was determined in patients given increasing levels of a single massive infusion at the end of 48 hours at 37 C. After the 100 mg. level of trypsin infusion was given, the clots of the patients showed fibrinolysis, whereas some samples presented fibrinolysis after the administration of 300 mg. and 400 mg. There was a slight but steady prolongation of the coagulation time from a five minute pretreatment level to eight minutes at the 400 mg. trypsin level, as determined by the Lee and White method. Patients given trypsin intravenously showed a drop in blood clot viscosity ranging from 10 to 30 centipoises as measured by the "ultra-viscoson" method (see figure). The maximal depression in blood clotting viscosities was obtained when doses exceeding 100 mg. per infusion were given. No agglutination occurred when in vivo trypsin-treated red blood cells were added to the serum of patients having the same blood group, and no increased agglutination occurred when anti-Rh serum was added to such cells. The same lack of response occurred when trypsin-treated serum was added to red blood cells of the same group. Thus, the erythrocytes of those patients who received trypsin behaved in a normal fashion, indicating that the red blood cells are not affected by antigenicity. The laboratory evidence is in accord with our clinical observations. Blood from trypsin-treated patients gave a negative Coombs' test reaction. No changes were noted either in the erythrocyte count or in the erythrocytes in the stained blood smears when taken prior to and following administration of trypsin.

CLINICAL RESULTS

Control Patients.—Patients with arteriosclerotic heart disease, hypertensive vascular disease, hypertrophy of the prostate, and diabetes mellitus comprised a control group. In this manner we established a base line in alterations in certain fundamental physiological aspects of the coagulation mechanism; we ascertained the nature and incidence of side-effects at various dose levels and determined the optimal rate of administration and enzyme concentration. With the exception of a sense of well-being that usually appeared during the first infusion, the administration of trypsin to these patients had no influence on the underlying illness or on factors comprising the clotting mechanism.

Patients with Acute Inflammatory Reactions.—The clinical results are summarized in the table. 1. Ischemic Leg Ulcers: Critical appraisal of any therapeutic agent given to patients with ischemic leg ulcers is difficult because of variable factors such as nutritional status, extent of arteriosclerotic involvement, duration and extent of the ulcerated area, degree of gangrenous change, and the presence of associated disease. In most instances, however, it was obvious that subsidence of the accompanying acute inflammatory reaction occurred following completion of the first few trypsin infusions. Liquefaction of exudates frequently followed the first infusion and was almost invariably present after subsequent infusions. During therapy eschars usually dropped off spontaneously or were readily removed revealing underlying areas of healthy granulation tissue. 2. Diabetic Gangrene: Considerable improvement in the inflammatory component followed the intravenous administration of trypsin to patients with diabetic gangrene of the feet. It is significant that the patients who responded well to trypsin



Comparison of "ultra-viscoson" curves before and after trypsin infusion.

therapy did not have extensive gangrenous involvement, although in each instance the accompanying deep cellulitis was rather widespread. The patient who was considered a therapeutic failure had widely disseminated areas of wet gangrene plus superimposed infection; an important trypsin-induced result was a nonextending line of demarcation between dead and viable tissue, which facilitated surgical separation. Each of the successfully treated patients was given daily intravenous infusions for five days. In one case separation of the gangrenous eschar occurred on the third day of treatment, and in some cases eschar separation occurred on the fourth day. On the fifth day following incision and drainage of fluctuant areas, considerable thin pus gushed forth. The follow-up treatment consisted of daily topical application of 100 mg. of trypsin powder with a no. 119 DeVilbiss atomizer and daily débridement of ulcerated areas. Healthy, abundant granulation tissue appeared on the 9th, 10th, and 15th days of treatment. It is critically important to treat ulcer areas with daily washings of Sorensen's phosphate buffer solution, followed by trypsin powder and mechanical removal of the loosened debris under sterile conditions. 3. Infected Diabetic Ulcers: Gratifying results, surpassed only by those seen in the postpartum thrombo-

phlebitis cases, were obtained in diabetic patients with cellulitis and ulceration of the feet or toes, but without extensive gangrene. It is interesting and probably significant that the first favorable signs elicited in the trypsin-treated thrombophlebitis and infected ulcer patients were of the same pattern. These included subsidence of edema in the involved part, restoration of healthy tissue color, improved mobility, and marked subsidence of pain.

4. Thrombosis of Central Retinal Vein: Ten of the 12 patients presented dramatic and prompt improvement as noted by restoration of vision, daily improvement in visual fields, blood coursing through the retinal vessels on exerting orbital pressure, subsidence of retinal edematous changes, and diminution in size of retinal exudates. Two patients who did not respond had pathological involvement of the longest duration, i. e., exceeding two months. Ten patients received 10 mg. of trypsin intravenously for three to seven days, while two successfully treated patients received trypsin intramuscularly. It is interesting to note that one of these patients had hypertensive vascular disease with a blood pressure of 240/160 mm. Hg.

5. Thrombophlebitis: These patients showed remarkable improvement. In fact the most striking and prompt results in the entire study were observed in patients with postpartum thrombophlebitis. In each instance subsidence of pain, edema, local heat, fever, leukocytosis, and Homans' sign, and a fall in sedimentation rate occurred within the first few hours after trypsin treatment. The dosage consisted of 10 mg. of trypsin per infusion twice daily for one to eight days. The minimal total quantity of infused trypsin associated with clinical improvement was 30 mg.; the maximum quantity of infused trypsin associated with unequivocal improvement was 220 mg. Patients in this study with post-thrombophlebitis syndrome benefited from complete courses of intravenously administered trypsin in that their chief disabling symptom, persistent edema of the involved extremity, improved considerably. In no instance did the edema disappear entirely. Nevertheless, the degree of improvement was sufficient to permit each patient to return to full-time employment. In three patients who were treated for thrombophlebitis associated with cancer of the pancreas (two) and prostate (one) thrombophlebitis of the uninvolved leg developed before completing successful treatment of the original phlebitis. Following further treatment the second thrombophlebitis cleared.

6. Thromboangiitis Obliterans: Patients with long-standing thromboangiitis obliterans received complete courses of intravenously administered trypsin. While no objective signs of improvement were observed, each patient stated that while under treatment there was lessening of rest pain and intermittent claudication. These symptoms recurred within four weeks of terminating therapy but were again relieved by biweekly injection of trypsin.

7. Coronary Occlusion: Three of the patients were considered to have recovered from recent myocardial infarctions prior to trypsin therapy except for frequent episodes of substernal discomfort. No untoward signs developed during the course of treatment or throughout subsequent periods, and anginal attacks occurred less frequently and were milder. In addition the patients' entire mental outlook became more cheerful. Three patients with more recent coronary occlusions were treated within 24 hours of the onset of acute symptoms. Each patient made an uneventful recovery. The evolution of the disease pattern in these few patients was characterized by clinical, laboratory, and electrocardiographic improvement. In these patients the intramuscular route of administration is preferred.

8. Acute Rheumatoid Arthritis: Following the first few intravenous infusions striking improvements were noted, including diminution of pain, decrease in swelling, increase in mobility of joints and functional capacity, and a marked sense of well-being. Where there had been extensive damage to the bones, residual deformities were unaffected. In two cases acute symptoms recurred four and six days, respectively, after treatment was completed. None of the other patients had a relapse. A maximal degree of over-all improvement occurred within 24 to 72 hours after therapy was started. Three patients required from 48 to 72 hours to show maximal improvement, and these were in the oldest age group, 52 to 64. The remaining 15 patients were less than 50 years old, and each showed maximal improvement within 48 hours of commencing treatment. The patient requiring the longest time to show improvement, 72 hours, was the oldest in the series (64 years), had his disease the longest (20 years), and had the lowest red blood cell count (2,900,000 per cubic millimeter of blood). Although treatment was continued for five more consecutive days in most instances, there was no correlation between the duration of treatment or total dosage and the ultimate degree of improvement. No toxic side-effects followed the use of intravenously administered trypsin in this study. Occasionally, mild symptoms of frequency in urination, slight epigastric pain, or slight throbbing headaches were elicited over a short period of time. It is evident from the laboratory and clinical results that decided and prompt improvement followed the intravenous administration of trypsin to patients with acute rheumatoid arthritis. While, generally speaking, the natural course of rheumatoid arthritis makes the evaluation of therapeutic agents for this condition exceedingly difficult, spontaneous improvement is usually a gradual phenomenon. The quick remission consistently affected by intravenously administered trypsin would seem to exclude the possibility of spontaneous variation.

SIDE-EFFECTS

The 538 patients studied in this series received a total of 6,456 trypsin infusions. When the drug is given slowly, the only side-effect is transient facial flushing and a sense of warmth, occurring in 12% of the patients treated and lasting for an average of two to three minutes. A direct relationship exists between the quantity of trypsin injected and the incidence and severity of reactions. Single infusions of more than 400 mg. of trypsin were associated with a high incidence of side-effects, which, as a general rule, were mild and transitory. Significantly, the 10 to 15 mg. level of individual trypsin infusions was clinically effective and presented negligible side-effects. During earlier stages of this investigation when considerably higher doses were employed mainly in a 50 to 250 mg. range, endophlebitis frequently oc-

curred at the site of infusion. The incidence of this side-effect has been reduced considerably since smaller trypsin doses have been used in the 10 to 15 mg. range per infusion. It is interesting that decreased prothrombin inhibitor levels were present in the few diabetic patients in whom local phlebitis developed, despite smaller dose levels. In more than 98% of the patients receiving trypsin intravenously in the small dose range, however, local phlebitis never developed. This group manifested prolonged prothrombin inhibitor levels. In these studies we did not employ anticoagulants in order to exclude therapeutic variables. Since making this report, however, we have occasionally employed anticoagulants together with intravenously administered trypsin in thrombotic patients; the dose of trypsin did not alter the prothrombin level.

REPORT OF CASES

CASE 1.—A 53-year-old white laborer entered Metropolitan Hospital, Welfare Island, with 8 by 14 cm. and 6 by 12 cm. infected ulcers on both legs that had been treated with periods of bed rest, at least four to six weeks, plus extensive local and systemic therapy; the ulcers were sufficiently changed for a few days to permit limited ambulation. An infusion containing 10 mg. of trypsin in 100 cc. of sodium chloride solution was given after the patient had been confined to bed for 12 days, at which time there was essentially no change in the infected ulcers since last seen at the hospital seven months previously. Two infusions, each containing 10 mg. of trypsin, were given daily for the following four days without the development of untoward reactions. On the third day of the treatment the patient stated his legs felt "warmer and much better," and objective evidence of improvement such as absence of purulent exudate and appearance of granulation tissue was evident on the fourth and fifth days. On the sixth day after institution of therapy the patient became ambulatory. When seen in the clinic four weeks later the ulcer on the right leg had remained healed and a smaller ulcer had appeared on the left leg. The latter was treated successfully with trypsin powder applied locally. Except for a slight recurrence of pain in the area of the small ulcer, the patient was greatly improved.

CASE 2.—A 49-year-old Jewish widow with known hypertension for many years was admitted to the hospital with blurring vision, which had occurred on awakening three weeks previously. This had been diagnosed by an ophthalmologist as thrombosis of the central vein of the retina. No visual improvement was noted prior to admission, and another ophthalmologist confirmed the diagnosis and visualized a thrombus in the superior temporal vein. Arterial but no venous pulsations were observed. The patient received 10 mg. of trypsin on May 16, 10 mg. divided equally in two doses on May 17, 10 mg. on May 19, and 10 mg. on May 21. Following the administration of the first 10 mg. of trypsin, vision was considerably improved and fundal examination revealed a return of the venous pulsation and blood flow. On admission finger counting was at 15 ft., whereas on discharge the vision was 18/100.

CASE 3.—A 21-year-old Puerto Rican housewife entered the hospital because of pain and marked tenderness of the right lower extremity of three weeks' duration. She was unable to walk because of pain and had been confined to bed continuously for the past two weeks. Four weeks prior to admission she delivered a healthy child following an uneventful gestation. One week post partum, the patient experienced pain in the right calf region associated with moderate swelling extending to the thigh. Physical examination revealed tenderness and 2+ edema of the entire right lower extremity. The right leg was much warmer than the left. The diagnosis was acute postpartum thrombophlebitis, and a course of intravenously administered trypsin was recommended. On the second day of treatment, and after having received four doses of 10 mg. of trypsin each, there was considerable subjective and objective improvement. Following an additional four infusions of 10 mg. each (eight infusions in four days), the patient was entirely symptom free and the signs of thrombophlebitis had completely cleared.

CASE 4.—A 58-year-old white man was admitted to the Metropolitan Hospital because of painful swelling of the lower third of the right leg for the preceding three weeks; in addition he had polyuria, polydypsia, and weight loss of 41 lb. (18.6 kg.) over the past month. Physical examination of the right leg revealed redness, swelling, and tenderness over the lower third, measuring 10 by 14 cm. Immediately superior to this erythematous zone a deeply situated, exquisitely tender cord-like structure was palpable. The diagnosis was thrombophlebitis, with a localized area of erythema. Treatment consisted of continuous bed rest plus a full course of trypsin administered intravenously, On March 13, five days after admission, two infusions of trypsin solution were given, each containing 10 mg. in 100 cc. of isotonic sodium chloride solution. This dose and frequency of daily administration were repeated on the following three days. At no time were reactions noted. On March 14, the discolored area became considerably lighter and less extensive and the cord-like structure was smaller and less tender. On the following day the patient stated that he felt better and wished to get out of bed; the area of discoloration on the right leg had become much smaller and lighter, and the cord-like structure had decreased in size and was less painful. On March 16, because of further subjective and objective improvement, he was permitted out of bed for the first time in almost a month. At this stage, after administration of eight infusions of trypsin over four days, therapy was discontinued. On March 20, there was no evidence of thrombophlebitis in the right leg and a follow-up examination made six weeks later revealed no recurrence of symptoms.

CASE 5.—A 30-year-old Puerto Rican housewife entered the hospital unable to walk owing to severe pain and tenderness over the lower medial aspect of the left thigh for the preceding three weeks. Examination revealed an irregular, crescentic, stony, hard, hot, tender mass on the inner aspect of the lower third of the left thigh. The surrounding skin was lichenose and erythematous. A diagnosis of thrombophlebitis was made, and after five days of bed rest plus anticoagulants without improvement a course of intravenously administered trypsin was recommended. On the first day of therapy two infusions of trypsin, each containing 250 mg., there was less pain in the thrombosed area, the mass was smaller and less tender, the overlying skin was less shiny and erythematous. The following day two infusions were given, each containing 250 mg., without producing unusual reactions despite the high dosage. This patient was treated early in the investigation when the usual single dose was 250 mg. On the third day the patient accepted the first 250 mg. but refused the second because she felt "cured" and accordingly signed a hospital release. A follow-up examination made at her home three days later revealed marked regression in the size of the thrombus as compared with the size on admission as well as practically complete clearance of the overlying erythema. The patient has been able to conduct her household duties uninterruptedly since returning home.

CASE 6.—A 37-year-old Puerto Rican woman was admitted to the Metropolitan Hospital because of massive, bilateral serpiginous-like masses on the medial aspect of both thighs. There was a three month history of painful swelling over the inner side of the left thigh, with onset one week before of a similar, but somewhat smaller, painful swollen, sausage-shaped mass along the inner side of the right thigh. Examination revealed an extremely tender, red, indurated area over the medial portion of the left midthigh, measuring 22 by 11.5 cm. Coursing through the center of the erythematous zone was a markedly dilated, firm, hard thrombotic vessel. A smaller mass was present on the medial side of the right thigh. A diagnosis was made of bilateral thrombophlebitis of both thighs. Treatment consisted of bed rest and a course of intravenously administered trypsin. On March 7, six days after admission to the hospital, 10 mg. of trypsin dissolved in 100 cc. of isotonic sodium chloride solution was given intravenously. At the conclusion of the infusion a slight chill occurred. On the following day there was less pain and redness of the left thigh and the right thigh remained painful and tender. Two 10 mg. trypsin infusions were then given and repeated on the following three days, March 9, 10, and 11, without the development of untoward reactions. On March 9 her condition was about the same; however, on

March 10 there was considerable decrease in the size and associated tenderness of the masses on both thighs and the area surrounding the erythema was much lighter and less extensive. On March 16 the patient was discharged considerably improved and ambulatory. At the follow-up examination, two weeks later, fluctuant tender masses were palpable over the inner sides of both thighs. Following incision and drainage, considerable sterile pus was evacuated from each area. At her visit to the clinic two weeks later both thighs appeared normal.

CASE 7.—A 42-year-old white truck driver was admitted to Nyack Hospital, Nyack, N. Y., complaining of severe, crushing, substernal and precordial pain of several hours' duration. On admission the temperature was 99.6 C, pulse rate 130, respirations 40, blood pressure 100/70 mm. Hg, white blood cell count 17,100 per cubic millimeter of blood, and sedimentation rate 40. The lungs were clear, the point of maximal impulse in the sixth intercostal space at the anterior axillary line, the heart sounds somewhat distant but of regular rhythm, and no thrills palpable. The liver was slightly enlarged, and the extremities were normal. The electrocardiogram showed recent myocardial infarction, anteroseptal type. Treatment consisted of seven trypsin gluteal intramuscular injections, each containing 5 mg. of the enzyme, plus sedation. After the first treatment on the day of admission the substernal and precordial pain subsided considerably, and only minor complaints of pain were noted throughout the remaining period of hospitalization. Serial electrocardiograms showed the usual subsiding pattern of myocardial infarction, and the sedimentation rate became normal on the fifth hospital day. Bed rest was maintained for three weeks.

CASE 8.—A 33-year-old woman had moderately severe rheumatoid arthritis for 24 months, affecting principally the knees, feet, ankles, wrists, and hands. Over a period of years treatment was unsuccessful and had consisted of physical therapy, blood transfusions, gold therapy, typhoid vaccine, and corticotropin (ACTH). Three days prior to admission her left knee became swollen. After three daily intravenous infusions of trypsin, each dose consisting of 10 mg. in 100 cc. of isotonic sodium chloride solution, the signs and symptoms of acute inflammation involving the left knee had subsided completely. In addition, there was, in general, less pain and stiffness in the other joints less acutely involved at the time. The range of motion of the fingers and wrists was increased considerably. This improvement had been maintained for the preceding two months.

CASE 9.—A 62-year-old white schoolteacher visited the office of one of us (I. I.) with the complaint of massive thrombi that had been present on the anterior abdominal wall for the preceding eight years. The patient stated that eight years previously, following an abdominal operation, thrombophlebitis developed with extensive and severe involvement of the left lower extremity. As a direct result of this phlebitis (probably extending into the vena cava, according to the family physician) numerous dilated venous channels appeared on the lower anterior abdominal wall. Six months after these venules were first apparent they became confluent and remained thrombotic ever since. The diagnosis at the time of instituting intravenous administration of trypsin eight years later were postphlebitis syndrome in the left lower extremity and extensive phlebothrombosis of the anterior wall of the abdomen. Treatment involved 10 daily trypsin infusions consisting of 10 mg. in 100 cc. of sodium chloride solution. The patient remained ambulatory throughout treatment. At the end of this course there was subsidence of edema of the left lower extremity. The confluent masses of thrombi on the anterior abdominal wall were still present, but appeared definitely smaller, more irregular, and softer. The patient returned for a follow-up examination four weeks later, at which time there was no longer any evidence of thrombosis of the anterior abdominal veins. During a six months' follow-up period the thrombi did not recur. Moderate edema of the left lower extremity has persisted.

DOSAGE AND INDICATIONS FOR TRYPSIN

In animal experiments, we have demonstrated that excessive blood trypsin levels can effectively destroy the clotting mechanism.[3] This varies with the individual animal as well as with the dosage. For purposes of clinical control, therefore, it is advantageous to check midway through each infusion for excess blood trypsin levels during the infusion. Two methods have been devised by us for determining the extent to which blood trypsin is present in excess quantities. The plasma antithrombin level is perhaps more closely linked with blood trypsin content than any other circulating antitryptic substance.[4] Moreover, since antithrombin is an unusually stable protein we have noted that decreasing antithrombin levels following intravenous administration of trypsin means concomitant proteolysis of other and less stable clotting moieties, including factor 5 and prothrombin.[5] The imminence or actual presence of peptone shock is apparently linked with the stage of extensive proteolysis of clotting moieties. Thus, maintenance of normal antithrombin levels is of critical importance. It should be stressed that our purpose was to lyse the fibrin content of thrombi without unduly compromising the coagulating mechanism. Citrated blood samples were obtained during the course of trypsin treatments for immediate "five minute incubation" antithrombin determinations. In this manner trypsin infusions became subject to careful and continuous control. It is gratifying to mention that none of the patients reported on in this series, including the few who earlier in our studies received as much as 750 mg. in a single infusion, demonstrated diminution in antithrombin titer. In dogs diminution in antithrombin was observed when larger doses of trypsin were employed. This significant observation is correlated with the fact that, despite clinically effective fibrinolysis, the coagulation mechanism in humans remains essentially intact following intravenous administration of trypsin in the prescribed dosage range and rate of administration.

The second laboratory method utilized routinely as a method for estimating the extent of proteolysis induced by trypsin is a test that we refer to as the "prothrombin inhibitor determination." In brief, the procedure involves the following steps: Introduction of 2.5 cc. of isotonic sodium chloride into a vial containing 10 mg. of crystalline trypsin.[5a] Withdrawal of 0.024 cc. of this trypsin solution with a tuberculin syringe, and adding it to 0.3 cc. of the patient's plasma. Determination by means of a stop watch and a wire loop the length of time for a fibrin strand to first appear. At 37 C (water bath) the average length of clotting time ranges from 25 to 30 seconds. A normal control determination with normal plasma is run simultaneously. It has been our observation that a patient undergoing trypsin therapy shows prolongation of the "prothrombin inhibitor time." If at any time this test reveals marked diminution in the prothrombin inhibitor time trypsin should be discontinued at once. All patients have prothrombin inhibitor time

3. Innerfield, I.; Angrist, A., and Benjamin, J. W.: Studies on Trypsin: I. The Anticoagulant Action of Trypsin, Gastroenterology **20**: 630-635 (April) 1952.

4. Innerfield, I.; Angrist, A., and Benjamin, J.: Plasma Antithrombin Patterns in Pancreatic Disturbances, Gastroenterology **20**: 417-429 (Dec.) 1951.

5. Innerfield, I.; Angrist, A., and Boyd, L. J.: Plasma Antithrombin Titer in Incipient and Advanced Liver Failure, Gastroenterology **20**: 417-429 (March) 1952.

5a. The National Drug Company, Philadelphia, has prepared a special 10 mg. trypsin vial for performing this test.

determinations prior to institution of trypsin therapy. Trypsin therapy contraindicated in patients with markedly decreased prothrombin inhibitor time prior to trypsin therapy.

The primary purposes of intravenous trypsin therapy are (1) to depolymerize long-chained protein molecules, i. e., hydrolysis of the fibrin molecule, (2) to decrease the viscosity of encapsulated fluid, (3) to augment phagocytosis, (4) to enhance the biochemical process of liquefaction of purulent debris and inspissated thick viscid mucus, and (5) to cause reversal of acute inflammatory processes. It is important to note that decreased blood clot viscosity, fibrinolysis, and effective lysis of intravascular thrombi followed intravenous administration of trypsin when done in the previously outlined fashion, without otherwise jeopardizing the coagulation system; clinically, the cardinal indication for trypsin is acute inflammation, regardless of etiology.

Thus far, contraindications to intravenously administered trypsin appear to include hepatic insufficiency, congestive heart failure, cachexia, hemorrhagic states, and conditions associated with necrosis of vital tissues and severe anoxia, such as in advanced pulmonary emphysema and pulmonary fibrosis. Markedly depressed prothrombin inhibitor levels are considered an absolute contraindication.

EFFECTS

Infiltration of the infusion into healthy tissue did not produce necrosis or sloughing owing to the adequacy of antitryptic substances present in all living cells. There does occur, however, a short painful sensation in the region of the infiltration. Sloughing of healthy tissue is produced by alpha, beta, and gamma chymotrypsin and not by trypsin. Sensitization phenomena following intravenous administration of trypsin have not been observed in this study. It is well recognized that proteins of low molecular weight, like trypsin, seldom produce sensitization phenomena; however, when intervals exceeding three weeks occur between intravenous courses of trypsin intradermal and conjunctival tests should be made prior to the reinstitution of therapy. Although no evidence of sensitivity reactions has been encountered in the follow-up clinical cases, it is recommended that under no circumstances should a second course of intravenously administered trypsin be given without testing for evidence of hypersensitivity.

The effect of increasing dose levels of intravenously administered trypsin on certain clotting constituents in dogs has been reported by us.[1] Continuation of this study with both rabbits and dogs has provided additional data and insight into the physiological effects of intravenously administered trypsin on the coagulation mechanism and has enabled us to develop a method for safely administering trypsin intravenously in man. Previous workers reported that trypsin was too toxic for intravenous use,[6] produced shock, necrosis and sloughing of tissue sensitivity reactions,[7] and intravascular coagulation.[8] It is possible, indeed probable, that the particular trypsin employed by these workers in 1942, 1944, and 1945 was far different from the highly purified crystalline product used in our experiments. The slightest contamination of trypsin with chymotrypsin or carboxypeptidase can produce serious side-effects following intravenous administration.

Intravascular coagulation following the intravenous administration of purified trypsin has not been observed by us during animal and human studies. Large doses of such trypsin have powerful anticoagulant effects.[2] Shock; death, and small intracardiac thrombi have been observed to follow massive, rapid intravenous administration of trypsin in rabbits; but shock did not occur and intracardiac thrombi were not seen when the enzyme concentration and the rate of administration were within specific prescribed limits.[1a] In order to appraise the anticoagulant and fibrinolytic effects of trypsin it should be stated that the clotting mechanism is merely one part of a more comprehensive "coagulation system." Under normal physiological circumstances the absence of intravascular clotting reflects the adequacy of circulating clot inhibitors. The fluid state of the blood stream is maintained through the participation of these clot inhibitors and other naturally occurring anticoagulants, comprising a highly effective over-all plasma proteolytic enzyme system. Yet, small doses of trypsin in vitro produce clots. The following hypothesis is applicable to the explanation of the differing action of in vivo and in vitro trypsin. As in all dynamic biological processes, moieties comprising the coagulation system are constantly being degraded and synthesized in vivo. Moieties consumed in in vitro clotting, or following in vitro proteolysis, obviously cannot be resynthesized. When trypsin in small doses produced clots in vitro, it does so by digesting the prothrombin inhibitor grouping; i. e., digestion of the inhibitor molecular grouping from the prothrombin molecule enables prothrombin to convert into thrombin autocatalytically. This suggests that prothrombin molecules are less susceptible to small doses of trypsin than prothrombin inhibitor groupings. It is further suggested that the prothrombin inhibitor molecule complex has a protein configuration and is not too long-chained; since it is so readily attacked by trypsin in small doses. Experimental evidence confirms this observation. If this were not so, that is, if prothrombin were not "coated" by a "precursor molecular grouping" small in vitro doses of trypsin would attack prothrombin at once. An excess of in vitro trypsin proteolyzes not only the prothrombin molecular inhibitors but also prothrombin itself, factor 5, and fibrinogen. Thus excess in vitro trypsin destroys all clotting substances. In vivo clotting cannot occur following small doses of trypsin, however, provided the synthesis and replacement rate of digested clot inhibitor groupings exceed the rate and extent to which these moieties are proteolyzed. The plasma proteolytic enzyme system, plasmin, antithrombin, antirennin, and chymotrypsin inhibitor substances, further vitiates possible intravascular clotting effects of intravenously administered trypsin within specific limits of trypsin concentra-

6. Tagnon, H. J.: Effect of Intravenous Injection of Trypsin on the Blood Coagulation Time in Hemophilia, Proc. Soc. Exper. Biol. & Med. **57**: 45-47 (Oct.) 1944.

7. Rocha e Silva, M.: The Histamine Theory of Anaphylactic Shock with Special Reference to Anaphylaxis in Rabbit, Arch. Path. **33**: 387-408 (March) 1942.

8. Tagnon, H. J.: The Nature of the Mechanism of Shock Produced by Injection of Trypsin and Thrombin, J. Clin. Investigation **24**: 1-10 (Jan.) 1945.

tion and rate of administration. Large doses of intravenously administered trypsin digest both clotting and anticlotting protein moieties of the coagulation system.[1a] Thus, under normal conditions, maintenance of a fluid circulation following the parenteral administration of small doses of trypsin reflects the capacity of the liver to regenerate clot inhibitor moieties either faster or just as fast as they are proteolyzed. If the dose of trypsin is steadily increased (continuous infusion), it is apparent that a level of enzyme concentration will be reached that exceeds the capacity to elaborate essential clotting moieties at a rate equal to that of proteolysis. It is precisely during this excessive enzyme dose range, as given to animals,[1a] that anticoagulant, fibrinogenolytic, and fibrinolytic effects of intravenously administered trypsin become apparent. It may well be that the relative size of the molecules of these coagulant and inhibitor moieties determines their selective action to trypsin. The simpler, shorter inhibitor molecules are readily formed by the liver and are rapidly replaced following degradation.

The activation of a blood proteolytic enzyme system by trypsin requires far smaller quantities of trypsin and recently has been reported by three groups working independently.[9] Clinical observations reported in this paper support and extend those views, namely that trypsin converts plasminogen into active plasmin. Trypsin in solution is known to deteriorate rapidly, losing 40 to 50% of its activity in the first three hours; yet for weeks after cessation of trypsin therapy routine blood findings indicate increased fibrinolysis and increased prothrombin inhibitor levels. Clinically, as for example, in the patient cited with varices of the abdominal wall, therapy with trypsin resulted in maximal alteration and eventual disappearance of massive thrombosis; however, the thrombolysis occurred several weeks after trypsin therapy had been terminated. Similarly, patients with postphlebitis syndrome or chronic thrombophlebitis of long duration often manifest subsidence of edema many weeks after cessation of the treatment. Since it is inconceivable that the minute doses of trypsin used per se could maintain activity for several weeks, the immediate trypsin activation of naturally occurring proteolytic enzymes, such as the conversion of plasminogen to plasmin, is postulated. Once activated, these proteolytic enzymes continue functioning for several weeks. It is entirely possible that clinical effects are due to activation of the proteolytic enzyme system, not trypsin at all.

COMMENT

The prompt and striking improvement observed in patients with ischemic purulent leg ulcers strengthens the view that parenterally administered trypsin significantly alters the inflammatory reaction. Similarly, signs and symptoms of cellulitis accompanying acute thrombophlebitis subsided promptly after administration of trypsin. Striking improvement also followed administration of trypsin in patients with retinal thrombosis. It is significant that in the patients who did not respond favorably retinal artery thrombosis had developed two months prior to institution of treatment. The patients who responded to treatment had venous thrombotic episodes two or three weeks before treatment was started. The 71 patients with thrombophlebitis, responding favorably to trypsin, showed diminution in size, shape and consistency of superficial thrombi in situ within 24 to 48 hours after commencing treatment. Thrombi were seldom observed or palpated two weeks after cessation of therapy. The extent to which this thrombolytic effect was related to trypsin per se, however, cannot be determined on the basis of observations presented in this paper. It is highly significant that the subsidence of edema, with trypsin administration, reduced mechanical obstruction of vascular channels, improved collateral circulation, and restored lymphatic drainage, thereby facilitating naturally occurring proteolytic and thrombolytic mechanisms. An enhanced proteolytic enzyme and thrombus substrate interrelation resulting in augmented thrombolysis is strongly suggested. It is noteworthy that in none of the thrombophlebitis patients treated with trypsin did pulmonary emboli develop during a follow-up of several months.

Since electrocardiographic and histological examination of rabbit and dog hearts following intravenous therapy with trypsin were negative and since side-effects were negligible, the drug was administered to patients with recent myocardial infarctions. It is significant that no untoward sign developed during the infusions or periods of observation. Since an important pathophysiological component contributing to extension of myocardial lesions is intracellular and extracellular edema, it is conceivable that trypsin-induced lysis of intracapillary and lymphatic thrombi may contribute toward reversing the accumulation of interstitial myocardial fluid, facilitating capillary blood flow, and hastening repair of the damaged myocardium. The reduction in the intracellular and extracellular myocardial edema may be decisive in preventing further occlusion of minute coronary vessels by eliminating the factor of mechanical compression. In spite of the definite improvement noted in the convalescent and acutely diseased coronary patients, further evaluation of parenterally administered trypsin must await a much larger series of patients and the results of extensive animal experiments now in progress.

Impressive results were obtained in 15 patients with acute rheumatoid arthritis and in 3 with acute rheumatic carditis.[9a] The ideal antirheumatic agent should consistently affect fundamental systemic and tissue alterations of the disease. The brilliant investigations of Stetson [10] correlate morphological changes of the rheumatic state, such as necrotizing arteriolar changes, hemorrhagic necrosis, pancarditis, and changes in interstitial fluid compartments, with the development of capillary thrombi

9. Lewis, J. H., and Ferguson, J. H.: Studies on a Proteolytic Enzyme System of the Blood: V. Activation of Profibrinolysin by Trypsin, Am. J. Physiol. **170**: 636-641 (Sept.) 1952. Kocholaty, W.; Ellis, W. W., and Jensen, H. F.: Report No. 68, Army Medical Research Laboratory, Fort Knox, Ky., 1951. Innerfield.[1a]

9a. An intensive study of the effects of parenterally administered trypsin on the manifestations of acute rheumatic fever is now in progress under the supervision of Dr. Lawrence J. Slobody, professor of pediatrics, and Dr. Leonard I. Luhby, assistant professor of pediatrics, New York Medical College.

10. Stetson, C. A.: Studies on the Mechanism of the Schwartzman Phenomenon: Certain Factors Involved in the Production of the Local Hemorrhagic Necrosis, J. Exper. Med. **93**: 489-504 (May) 1951.

consisting of platelet masses and sticky leukocytes. These pathophysiological changes constitute morphological alterations of the Schwartzman and Arthus type.[10] It is entirely possible that the almost immediate therapeutic response of patients with acute rheumatoid arthritis and acute rheumatic carditis to trypsin is based on lysis of intracapillary and lymphatic thrombi in areas undergoing the Schwartzman or Arthus type of tissue reaction.[11] Therefore, parenterally administered trypsin provides the means for suppressing and reversing this type of tissue hypersensitivity reaction. In a previous investigation we have reported observations on the anticoagulant, fibrinolytic, and thrombolytic properties of intravenously administered trypsin; thus, it seems plausible to assume that intracapillary and lymphatic "plugging" in areas undergoing hemorrhagic necrosis would be lysed by the administration of trypsin. Certainly, the almost immediate subsidence of edema after institution of this therapy in patients with acute rheumatic arthritis is compatible with restitution of lymphatic drainage, improvement in local circulatory integrity, and changes in fluid electrolyte and hydrogen ion concentration.

SUMMARY AND CONCLUSIONS

There was dramatic subsidence of all signs and symptoms of acute inflammation in 94.3% of the patients studied during this investigation. It therefore appeared likely that, in a manner as yet unexplained, trypsin activated a system of naturally occurring enzymes, which participate in determining the rate at which inflammatory processes subside, thereby enabling healing to follow. Trypsin, then, alters the host reaction to injury. Studies now in progress in our laboratory indicate that this augmented host reaction to tissue injury, initiated by trypsin, embraces such factors as (1) enhanced surface and intravascular phagocytosis, (2) increased lysis of liquefied bacteria, (3) decreased viscosity of all tissue fluids, (4) lysis of intralymphatic thrombi, (5) dissolution of fibrin barriers in areas of acute inflammation, (6) liquefaction of capillary thrombi consisting of leukocytes and platelet masses, and (7) amelioration of metabolic defects in the areas of acute inflammation, i. e., elevation of hydrogen ion concentration and inhibition of anaerobic glycolysis. There then follows restoration of "metabolic continuity" with the remainder of the organism occasioned by lysis of capillary thrombi in areas of acute inflammation. The end-result is rapid suppression and reversal of the signs and symptoms of acute inflammation. It would therefore appear that, expressed simply, the rate at which proteolytically activated biochemical reactions occur determines in large measure the subsidence rate of the acute inflammatory reaction. That trypsin apparently activates this proteolytic enzyme system seems substantiated in this investigation. From a therapeutic standpoint, then, trypsin plays a significant role in catalyzing enzymatic sequences that augment the host reduction to injury.

983 Park Ave. (Dr. Innerfield).

11. Experiments now in progress indicate that trypsin suppresses the Schwartzman phenomenon in rabbits.

CLINICAL NOTES

USE OF TRYPSIN INTRAVENOUSLY IN A GUNSHOT WOUND

REPORT OF A CASE

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The use of trypsin (Enzar) intravenously in thrombophlebitis was reported in the *Bulletin of the New York Academy of Medicine* of August, 1952. The following case report is intended to encourage clinical use of trypsin intravenously in traumatic wounds and compound fractures, especially in war wounds. The case described illustrates the potentiality of this substance as regards (1) removal of debris, (2) decrease of edema, (3) removal of slough, (4) lessening of drainage, (5) decrease in exudate, (6) anticoagulant and fibrinolytic action, (7) removal of medium for bacteria, and (8) speeding up of the entire healing process.

REPORT OF CASE

A 26-year-old white man was accidentally struck by a rifle bullet in the left arm while hunting in Maine on Oct. 26, 1952. The bullet entered the lateral aspect of the upper arm and made its exit on the medial aspect, taking a piece of skin about 3 by 2 in. (8 by 5 cm.) in size with it. The humerus was split obliquely. Fortunately, no major nerve or blood vessel was severed.

An emergency hanging cast was applied in Maine on Oct. 26, 1952. On Nov. 1 the patient was admitted to the Clara Maass Memorial Hospital in Newark, N. J. On admission the wound was draining profusely, and the arm was three times its normal size. Openings at the site of the entrance and exit wounds exposed the fractured bone. The patient had been receiving penicillin and streptomycin. This therapy was continued, and traction was instituted by means of an airplane splint and a Steinmann pin (through the ulna below the olecranon), with a clevis attached to the lateral extension of the airplane splint.

There was no improvement in the edema, slough, drainage, exudate, and necrosis for several days. The patient was treated with trypsin intravenously (50,000 units in 200 cc. of isotonic sodium chloride solution given slowly, daily). He showed no outward reaction. On the third day of intravenous trypsin therapy, the edema had subsided considerably, the drainage was moderate, the necrotic tissue had become demarcated (and was removed), and the bullet holes had begun to close. On the sixth day the edema had disappeared, the wound was clean, drainage had ceased, exudate was minimal, and the edges of the wound looked fresh and healthy.

The wound progressed to complete healing, with strong callus formation at the site of union. The traction pin was removed three weeks after insertion. Six weeks from the occurrence of the compound fracture, the arm was in excellent condition, the fracture was united, and the wounds were closed. No grafting was necessary. The splint was removed, and the arm was placed in a triangular supportive bandage without a dressing.

CONCLUSIONS

The rapidity of healing in this case can be attributed to (1) the digestive action of the trypsin, (2) the proteolytic action on necrotic tissue, (3) the denial of a medium (debris and slough) to bacteria, (4) the anticoagulant action of trypsin, and (5) the opening up of

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humoral channels of supply and excretion in the devitalized area. The potential proteolytic and fibrinolytic and anticoagulant properties of trypsin unquestionably need further clinical trial. Intravenous use of trypsin in one case does not present any conclusive evidence in favor of use of this enzyme as an acceptable form of treatment of wounds. The results in this case (without any adverse reaction) are of such a nature, however, as to encourage further clinical studies of the intravenous use of purified trypsin in traumatic or infected wounds.

234 Mt. Prospect Ave.

SEVERE PARA-AMINOSALICYLIC ACID HYPERSENSITIVITY SIMULATING MONONUCLEOSIS OR HEPATITIS

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and
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Thousands of tuberculous patients are now using *p*-aminosalicylic acid as an adjunct in the chemotherapy of their disease. The commonest side-effect noted with this drug has been gastrointestinal irritation,[1] which occurs in about 10% of the patients. A smaller number of patients exhibit fever and a skin rash [2] after several weeks of therapy. A severer form of hypersensitivity to *p*-aminosalicylic acid, which may simulate mononucleosis [3] or hepatitis,[4] has recently been described in the foreign literature. One of these cases was fatal.[5]

Eight patients exhibiting this severe type of hypersensitivity to *p*-aminosalicylic acid have been encountered among approximately 3,000 patients who have taken the drug in this institution over the past few years. It is most important that the condition be recognized and therapy stopped promptly, since a mistaken diagnosis of mononucleosis or hepatitis may result in continued therapy with *p*-aminosalicylic acid, followed by greater morbidity and perhaps death.

CHARACTERISTICS OF THE REACTION

In the eight cases studied the clinical and laboratory characteristics of the reaction were as follows:

Onset.—The reaction began 23 to 37 days after the start of *p*-aminosalicylic acid therapy. Fever ranged from 101 to 105 F. Chills accompanied the fever in all but one case and were severe in two cases. The complaints of headache and generalized aching were made by half of the patients. Six patients complained of nausea, and in three of these it was accompanied by emesis. Burning of the eyes and lacrimation occurred in five patients. A skin rash developed in all cases. The rash involved the face, neck, and arms in the milder cases and was generalized in the severer ones. Usually it was erythematous and macular, but in one case it was urticarial. The pruritus was fairly severe in all but one patient. Cervical lymphadenopathy was noted in five patients. Axillary lymph nodes were also palpable in one patient and inguinal nodes in another. Hepatomegaly with tenderness and splenomegaly were noted in two patients. One of these had obvious jaundice, with a bilirubin level of 4.6 mg. per 100 cc.

Laboratory Studies.—The most interesting finding was the presence of atypical lymphocytes varying from 1% to 21%. These lymphocytes corresponded to those described as type 1 and type 3 by Downey [6] or as virocytes by Leibowitz.[7] Neutropenia, left shift, toxic granulation, relative or absolute lymphocytosis, and eosinophilia (11% to 50%) were also commonly noted. Cold agglutination tests and Paul-Bunnell reactions (repeatedly performed in each patient) were consistently negative.

Alkaline phosphatase values were above normal in three of the four cases studied (13.7 units, 21.4 units, and 52.6 units). Thymol turbidity tests were above normal in three of five cases studied (5 units, 8 units, and 19 units). Bilirubin was above normal in three of five cases studied (1.9 mg., 1.4 mg., and 4.6 mg. per 100 cc.). The cephalin flocculation test was 3 or 4 + in the five cases studied. The sulfobromophthalein (Bromsulphalein) test was performed in three patients; one showed 5% (normal) and the other two 15% and 20% retention.

Scratch, intradermal, patch, and passive transfer tests were performed. The most useful of these was the patch test, which was frequently positive when performed by applying a 33% ointment of *p*-aminosalicylic acid in lanolin to the intact skin for 48 hours.

Clinical Course.—When administration of the drug is discontinued, the fever, rash, lacrimation, and itching subside rapidly in the course of a few hours to a few days. The blood picture reverts to its previous condition in a week or two. The sulfobromophthalein test returned to normal within a month in the two patients mentioned (15% and 20% retention). Exacerbation of symptoms, reappearance of atypical lymphocytes, increase in eosinophils, and neutrophilic left shift occur promptly if the drug is readministered even in fractional doses.

COMMENT

The sudden onset of fever with adenopathy and atypical lymphocytes suggests the possibility of infectious mononucleosis. Nausea, emesis, hepatomegaly, splenomegaly, and abnormal liver function tests strongly suggest the possibility of hepatitis. While studies are being made to verify the presence or absence of these conditions, the patient may become progressively worse if *p*-aminosalicylic acid therapy is continued. It is therefore of considerable importance that the true origin of the clinical picture should be recognized early. Fever, rash,

From the Municipal Tuberculosis Sanitarium.

1. Nagley, M. M., and Logg, M. H.: Para-Aminosalicylic Acid (P.A.S.) in Pulmonary Tuberculosis, Lancet **1**: 913-916 (May 28) 1949. Madigan, D. G., and others: Para-Aminosalicylic Acid in Tuberculosis: Clinical and Pharmacological Aspects, ibid. **1**: 239-245 (Feb. 11) 1950.

2. (*a*) Kierland, R. R., and Carr, D. T.: Reactions to Para-Aminosalicylic Acid, Proc. Staff Meet., Mayo Clin. **24**: 539-543 (Oct. 12) 1949. (*b*) Warring, F. C., Jr., and Howlett, K. S., Jr.: Allergic Reactions to Para-Aminosalicylic Acid: Report of 7 Cases, Including 1 Case of Löffler's Syndrome, Am. Rev. Tuberc. **65**: 235-249 (March) 1952.

3. Sjoukes, P.: Clinical Picture Resembling Infectious Mononucleosis Caused by Para-Aminosalicylic Acid, Nederl. tijdschr. geneesk. **3**: 2001-2006 (Aug. 16) 1952. Randolph, T. G., and Gibson, E. B.: Blood Studies in Allergy: Presence in Allergic Disease of Atypical Lymphocytes and Symptoms Suggesting the Recovery Phase of Infectious Mononucleosis, Am. J. M. Sc. **207**: 638-643 (May) 1944.

4. Cuthbert, J.: Acquired Idiosyncrasy to Sodium *p*-Aminosalicylate, Lancet **2**: 209-211 (Aug. 5) 1950. McKendrick, G. D. W.: Toxic Hepatitis from Para-Aminosalicylic Acid, ibid. **2**: 668-669 (Oct. 13) 1951. Steel, S. J.: Acquired Sensitivity to Para-Aminosalicylic Acid, Brit. M. J. **1**: 415-416 (Feb. 23) 1952.

5. Muri, J.: Lethal *p*-Aminosalicylic Acid Intoxication, Nord. med. **47**: 155-157 (Feb. 1) 1952.

adenopathy, and lacrimation constitute a syndrome frequently found in drug hypersensitivity and should therefore awaken suspicion. It is necessary to know, in addition to these findings, that *p*-aminosalicylic acid hypersensitivity can cause the appearance of atypical lymphocytes and also evidence of liver damage. If the clinician is aware of these facts, he will recognize or suspect *p*-aminosalicylic acid hypersensitivity and promptly stop administration of the drug. Proof that the syndrome described is a hypersensitivity reaction is afforded by the fact that it recurs even after a long interval on readministration of very small doses of the drug.

Since the patients are almost always receiving streptomycin therapy concurrently, the reaction is frequently attributed to this drug; however, all of my patients have been able to continue taking streptomycin without difficulty after *p*-aminosalicylic acid therapy was discontinued and the reaction had subsided. Rare cases have been noted in which the hypersensitivity reaction recurs on readministration of either drug alone.[2b]

Treatment may be attempted by the use of antihistaminics. In my experience, this has not been effective enough to permit continued therapy. Desensitization, after the symptoms have subsided, has been reported successful in about 50% of the cases. My attempts have not been that successful. If tried, treatment should start with drop doses orally and increased very slowly.

p-Aminosalicylic acid is used with streptomycin mainly because it delays the emergence of resistant tubercle bacilli. Isoniazid or oxytetracycline (Terramycin) may be used as a substitute to accomplish this purpose in patients who cannot take *p*-aminosalicylic acid.

SUMMARY

A recently recognized syndrome caused by severe hypersensitivity to *p*-aminosalicylic acid is described. In addition to fever, rash, lymphadenopathy, and lacrimation, a blood picture simulating early infectious mononucleosis and evidence of liver involvement simulating hepatitis is noted in these patients. The symptoms subside promptly on withdrawal of the drug and recur if it is readministered. It is important not to mistake the syndrome for mononucleosis or hepatitis, because continued administration of the drug causes severe morbidity and may be fatal.

5601 N. Pulaski Rd. (Dr. Lichtenstein).

6. Downey, H., and Stasney, J.: Infectious Mononucleosis: Hematologic Studies, J. A. M. A. **105**: 764-768 (Sept. 7) 1935. McKinlay, C. A.: Infectious Mononucleosis: Clinical Aspects, ibid. **105**: 761-764 (Sept. 7) 1935.

7. Leibowitz, S.: Infectious Mononucleosis: Value of Differential Absorption Tests in its Serologic Diagnosis, Am. J. Med. **13**: 172-182 (Aug.) 1952.

Liver Function Tests.—Careful clinical evaluation of jaundiced patients is of great importance since blind acceptance of results of liver function tests may be misleading. The alkaline phosphatase and flocculation tests are helpful in deciding whether jaundice is hepatocellular in origin or caused by extrahepatic bile duct obstruction. Phosphatase activity of 30 or more King-Armstrong units strongly suggest obstructive jaundice. Conversely, positive results of flocculation tests indicate intrinsic hepatic disease. Use of this combination provided correct diagnosis in 72% of 54 jaundiced patients at Guy's Hospital, London. In 3 cases, the results were misleading and in 12, the two tests were valueless. Alkaline phosphatase is apt to exceed 30 King-Armstrong units with malignant biliary obstruction.—S. Weiss, M.D., Jaundice, *Review of Gastroenterology*, October, 1952.

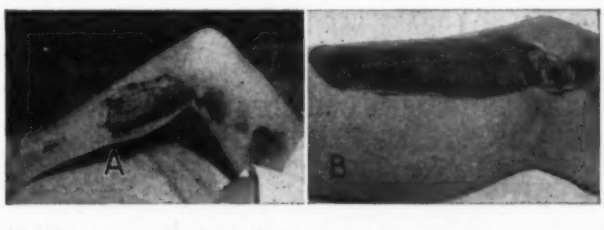
ULCERATION OF THE SKIN FOLLOWING INTRAVENOUS USE OF ARTERENOL

Joseph F. Uricchio, M.D.
Daniel G. Calenda, M.D.
and
Frank B. Cutts, M.D., Providence, R. I.

Tissue necrosis and ulceration of the skin have previously been reported as complications following the use of arterenol (3, 4-dihydroxyphenylaminoethanol).[1] Recently, we had occasion to observe a patient in whom similar lesions developed after the intravenous administration of this pressor amine into the right ankle. The drug was given, in this instance, to maintain blood pressure after an intestinal resection for gangrene of the bowel secondary to mesenteric vascular occlusion.

REPORT OF A CASE

A 48-year-old white married man had had 13 previous admissions to the Rhode Island Hospital. In February, 1951, he was admitted because of severe intermittent claudication. A left lumbar sympathectomy was done. At operation no pulsations were noted below the bifurcation of the aorta, and the diagnosis of osteoporosis due to trauma was made. The following month the patient was admitted because of chest pain. An electrocardiogram gave evidence of acute coronary insufficiency. In March, 1951, a right lumbar sympathectomy was performed, and in June of that year a left midthigh amputation was carried out because of symptoms and signs of marked peripheral arteriosclerosis. In September, 1952, the patient was treated for acute lateral myocardial infarction. On Dec. 5, 1952, he noted crampy pain in the midabdomen associated with vomiting and diarrhea. On examination, his temperature was 98 F, pulse 120 and irregular, and blood pressure 150/110 mm. Hg. Auscultation of the heart revealed the presence of auricular fibrillation, which was confirmed by electrocardiogram. Initially the abdomen was relaxed. During the succeeding hours increased tenderness and rigidity developed in his abdomen, associated with the disappearance of peristalsis. The white blood cell count was 39,000. On Dec. 6, 1952, an ileotransverse colostomy was performed because of gangrene of the small bowel secondary to a superior mesenteric artery occlusion. During the course of the surgery, the patient was given *l*-arterenol (Levophed) into the right arm, 4 mg. dissolved in 1,000 cc. of dextrose in water and given at the rate of 20 drops a minute. The blood pressure was maintained satisfactorily. Postoperatively, the patient was digitalized and given quinidine intramuscularly. In addition, a cut was made at the right ankle and a cannula inserted. A transient bout of



Right lower extremity showing ulceration and necrosis of tissue, (*a*) view along the course of the long saphenous vein and (*b*) a more detailed view of the area of ulceration about the knee.

From the Heart Station, Rhode Island Hospital.

1. Greenwald, H. P.; Gootnick, A.; Luger, N. M., and King, J. A.: Tissue Necrosis Following Subcutaneous Infiltration with Nor-Epinephrine, New England J. Med. **246**: 252 (Feb. 19) 1952. Kurland, G. S., and Malach, M.: The Clinical Use of Nor-Epinephrine in the Treatment of Shock Accompanying Myocardial Infarction and Other Conditions, ibid. **247**: 383 (Sept. 11) 1952.

hypotension developed, and arterenol was infused through the plastic cannula at the rate of 20 drops a minute. This was discontinued after a total of 100 cc. was given, and the blood pressure became stable. Within 24 hours ulcers and blebs began to develop along the course of the right saphenous vein (see figure). These lesions progressed and became intolerably painful. Superficial gangrene appeared, which subsequently extended to the subcutaneous tissues. On Jan. 3, 1953, a right midthigh amputation was performed.

COMMENT

Arterenol is being employed with greater frequency in the treatment of peripheral vascular collapse. One of the effects attributable to its use has been local venospasm and phlebitis. Superficial vesicular eruptions and ulceration may then develop. The process may progress to gangrene. Conservative therapy is usually successful in the management of these complications; however, in the presence of peripheral vascular disease, one may not observe complete healing. Such has been our experience in this case. While the infusion of arterenol by means of a plastic cannula may be of value in preventing local extravasation, it does not prevent the development of venospasm and tissue necrosis. It is noteworthy that in this case arterenol was administered in an upper extremity without sequelae. Thus, in the presence of occlusive vascular disease, this drug should be used with extreme caution, if at all, and should be given in one of the arms.

NEUROLOGICAL COMPLICATIONS FOLLOWING THE USE OF "EFOCAINE"

REPORT OF THREE CASES

Sidney K. Shapiro, M.D., Minneapolis
and
David D. Norman, M.D., Bethesda, Md.

"Efocaine," a long-acting local anesthetic, a product of E. Fougera & Co., has been publicized widely and is being used freely by the medical profession. "Efocaine" is a solution containing 1% procaine, 0.25% procaine hydrochloride, and 5% butyl-*p*-aminobenzoate in a solvent composed of 2% polyethylene glycol-300, 78% propylene glycol, and water. It is preserved with the usual preservatives, 0.1% sodium metabisulfite, and phenylmercuric borate (1:25,000). Bonica [1] has recently reported his experience with the use of "efocaine" in 100 patients. In six of these patients, postinjection neuritis and pain were encountered. He does not give details as to the seriousness or duration of disability in these patients. We have recently encountered three cases in which serious neurological residuals have resulted from the use of "efocaine." The purpose of this report is to urge caution in the use of this drug.

REPORT OF CASES

CASE 1.—On Sept. 9, 1952, a 34-year-old white man had the apical and posterior segments of the upper lobe of his right lung resected for tuberculosis. On Oct. 1, a second segmental resection of the upper lobe of the right lung was carried out. On this occasion the patient was placed in the usual three-fourth semiprone position, with the incision being made through the previous thoracoplasty scar. The second and third ribs were removed, and a more extensive resection was carried out without incident. At the conclusion of the procedure, 1 cc. of "efocaine" was deposited about the intercostal bundles in the region of the tips of the transverse processes from the second through the seventh thoracic segments. Approximately eight hours after surgery, the patient became aware of the fact that he was unable to move his legs and was numb from the nipple line down. He became incontinent of urine and feces.

On Oct. 2 the neurological examination revealed the presence of transverse myelitis with a sensory level at the fourth thoracic segment. Position sense was absent in the lower extremities. Deep tendon pain was intact. There was complete paralysis of all the muscles of the right lower extremity. In the left lower extremity, there was a trace of function in the hip flexors but the remainder of the musculature was completely paralyzed. The deep reflexes in the lower extremities were hyperactive. The toe signs were negative. When the patient was reexamined four weeks later, there had been only slight improvement in his neurological status. The findings were essentially unchanged except for the slight return of function in scattered muscle groups in the left lower extremity. A minimal dorsiflexion of the right big toe was the only movement in the right lower extremity. A sustained patellar and ankle clonus had developed bilaterally. At the time of writing (Nov. 29), the patient continued to be paraplegic and the urinary incontinence had persisted.

Comment.—It was the opinion of the operating surgeon that, owing to the obliteration of landmarks by the previous surgery, a portion of the "efocaine" deposited at the fourth rib level had found its way intrathecally. Severe transverse myelitis developed, resulting in paraplegia due to use of the "efocaine."

CASE 2.—A 32-year-old white woman on Sept. 14, 1952, while in labor received a paracervical injection of "efocaine" in an effort to block the pelvic nerves bilaterally. Coincident with the injection, she noted immediate numbness of the left leg. The patient delivered uneventfully. The numbness improved somewhat but persisted from the left knee down. On Sept. 19, she began to complain of sharp shooting pains and constant aching of the left lower extremity. When examined on Sept. 24, she demonstrated the following positive neurological signs: There was moderate weakness of the left quadriceps, hamstrings, everters of the foot, and dorsiflexors of the ankle and toes. The left ankle was markedly swollen, and the patient reported that this swelling increased when she was on her feet for any length of time. Reddish discoloration and excessive perspiration of the dorsum of the left foot were present.

When she was last seen on Oct. 29, some improvement had occurred in the patient's condition. The pain had responded to the use of priscoline® (2-benzyl-2-imidazoline), 50 mg. three times a day, and physical therapy. The swelling of the foot and ankle, while still present, was less marked. The muscle weakness demonstrated on the initial examination persisted.

Comment.—The lumbosacral plexus was involved at the time of the injection of the "efocaine" in this case. This involvement resulted in toxic neuritis, which is still partially disabling to this patient.

CASE 3.—A 36-year-old white man was operated on for a solitary lesion in the upper lobe of the right lung on Sept. 8, 1952. The fifth rib on the right side was resected from a point just proximal to the tip of the transverse process to the midaxillary line. After the completion of the operation, 2 cc. of "efocaine" was instilled in the region of the intercostal bundle at the angle of the ribs from the third to the seventh thoracic

From the division of Neurology, University of Minnesota (Dr. Shapiro). Fellow, National Institute of Neurological Diseases and Blindness (Dr. Norman).

1. Bonica, J. J.: Management of Intractable Pain with Analgesic Blocks, J. A. M. A. **150**: 1581-1586 (Dec. 20) 1952.

segment. Twelve hours postoperatively, the patient noted anhidrosis on the right side involving the right side of the face and body extending down to the right groin. This anhidrosis was complete above the level of the umbilicus, and partial from the umbilicus to the groin. This condition was still present on Nov. 28.

Comment.—Following the use of "efocaine," evidence of involvement of the sympathetic nervous system developed and has persisted in this patient. The involvement was manifested by anhidrosis on the right side.

SUMMARY AND CONCLUSIONS

Three cases have been reported in which, following the use of "efocaine," serious neurological symptoms developed and persisted to the time of writing. Following the use of this drug, in case 1 transverse myelitis developed, in case 2 a lumbosacral neuritis, and in case 3 involvement of the sympathetic nervous system. The use of "efocaine" should be sharply restricted and cognizance taken of the potentially serious nature of the neurological complications following its use.

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ARACHNIDISM TREATED WITH CORTISONE

REPORT OF A CASE

Z. Maretić, M.D., Pula, Yugoslavia

During recent years bites of the Latrodectus tredecimguttatus spider have been encountered frequently in Istria, Yugoslavia. During the period 1948-1952 in the General Hospital of Pula, 101 patients were treated for this condition. The persons bitten by the spider show [1] a disturbed general condition with severe pains, especially in the loins, abdomen, and extremities, convulsions, tachypnea, pressure in the chest, vomiting, excessive perspiration and salivation, and rigidity of abdominal muscles. The tendon reflexes and the pressure of cerebrospinal fluid are increased, and changes in the fundus of the eye are, in some cases, marked. The patients have hyperemia of the face, edema of the eyelids, and conjunctivitis, and show increased blood pressure, oliguria, albuminuria, abnormal values of urea blood concentration and urine dilution, and temporarily disordered liver metabolism. In some cases some days afterward a rash appears. In regard to other symptoms the local findings are relatively insignificant. To a degree signs of the alarm reaction have been noted in my patients. This is demonstrated by changes in the hemogram, with the appearance of leukocytosis, fall of eosinophils, neutrophilia and lymphopenia, increase in excretion of rest nitrogen, hemoconcentration, changes in the glucose curve and values of electrolytes in patients, as well as the pathological macroscopic and microscopic findings in the organs of experimental animals: enlargement of the adrenals, and enlargement of the cortex with thin zona glomerulosa and enlarged zona fasciculata and zona reticularis. For these reasons cortisone therapy was used in the case herein reported.

A country man from Poreč, aged 52, entered the General Hospital of Pula July 24, 1952. About 24 hours previously, when he was sleeping on the straw after threshing, he awoke because of pain radiating from the right knee into the groin. Shortly afterward the pain became intense and moved to the abdomen, chest, and loins. He noted paresthesia and burning in his feet, especially in the soles. The pains seemed to be pressing and cutting in the loins. He was rather warm and felt as if he would "burst." The patient shivered, threw himself from side to side, was sweating extremely, and could not speak. He did not urinate for 15 hours. He vomited three times and had heartburn and highly increased salivation.

The general condition was poor, and the patient could not stand on his legs. A fear of death was noted. Respirations were 30 per minute, superficial, and groaning. The temperature was 36.7 C, pulse 84 per minute, and blood pressure 160/120 mm. Hg. His face was hyperemic, the conjunctivas were injected, and the eyelids and loose tissue below the eyes manifested slight edema. The abdomen was slightly distended, the abdominal musculature rigid, and the liver palpable for ½ fingerbreadth and sensitive to pressure. On the medial side of his right knee there was a sharply limited red spot, the diameter of which was 1 cm. The sensitivity to needle stings was diminished in this region. The fibrillation of musculature in the right leg was marked.

The abnormal laboratory findings were as follows: leukocytes 12,400, eosinophils 56 per cubic millimeter, and urea nitrogen in blood 72 mg. per 100 cc. The white blood cell study showed slight neutrophilia and lymphopenia. A thymol test and a hematocrit gave above normal results. Fifteen minutes after admittance, at 3:15 p. m., the patient, who weighed 58 kg., received 80 mg. of cortisone (Cortone) acetate intramuscularly. Twenty minutes later amelioration was noticed; the patient was quieter, did not throw himself about, and breathed easier. After one hour he said that the formerly intense pain in the loins had disappeared and slight pain remained only in the abdomen. Still he had disturbances in his feet. According to my observations, of all the symptoms foot disturbances are most resistant to therapy and persist the longest in patients. Relief became more manifest every hour. At 5:30 p. m. the patient felt no disturbances except for slight pain in his feet. Objective amelioration was also observed. The patient was completely quiet, the rigidity of abdominal musculature had disappeared, the edema of the eyelids was less, and the breathing was quiet; respirations were 20 per minute, and blood pressure, 120/85 mm. Hg. At midnight the patient had a relapse of pain, but afterward he felt well and slept. Sleeplessness was observed as a constant symptom in my patients. The next day the patient was well, and during the following days the laboratory and other findings returned to normal. On July 26 a slight morbilliform rash appeared on his abdomen.

CONCLUSIONS

Greiner [2] included the bites of venomous animals, such as Latrodectus tredecimguttatus, among diseases in which corticotropin (ACTH) and cortisone "appear to be of great value." In this case I am of the opinion that a somewhat larger dose of cortisone, and possibly two such doses, would have given a still better effect. It is evident that for successful treatment of arachnidism one can also use less expensive drugs, but in severe cases or in those patients who are in danger of death cortisone possibly combined with calcium gluconate or antivenin would be of greater value. In the case reported, arachnidism with manifest signs of alarm reaction was successfully treated with a single dose of 80 mg. of cortisone.

Opća bolnica.

The cortisone acetate used in this study was manufactured by Merck & Company, Inc., Rahway, N. J.

1. Maretić, Z.: Beobachtungen über Pathologie und Klinik des Latrodektismus in Istrien (1948-1950), Acta trop. 8: 136-144, 1951.

2. Greiner, T.: Current Uses of Cortisone and ACTH, Am. J. M. Sc. 223: 553-568, 1952.

INSTRUMENT FOR CONTINUOUS RECORDING OF BODY TEMPERATURE

Robert M. Weiss, M.D.
and
Charles B. Ripstein, M.D., Brooklyn

Artificial induction of low body temperature in patients undergoing cardiac surgery and in the treatment of hyperpyrexia has emphasized certain technical problems in clinical thermometry. The standard clinical thermometer, although adequate for the majority of studies, is not well suited to the newer methods for the production and maintenance of the hypothermic state. There are difficulties involved in reading the body temperature during surgical procedures and in the management of neurosurgical patients who require careful temperature control. The ideal instrument for these purposes should possess certain qualifications. It should be highly accurate and simple to operate and interpret, and it should give a continuous record. In addition, it should be rugged and portable for use in the operating room and on the ward. We believe that the instrument described in this paper fulfills these specifications and represents a distinct advance in clinical thermometry. Previous attempts to produce such an apparatus have been conducted along the lines of thermocouple-galvanometer combinations with direct reading scales.[1] While such units possess a high degree of accuracy, they do not give a continuous record, and they require the personal attention of the observer to balance the galvanometer for each reading.

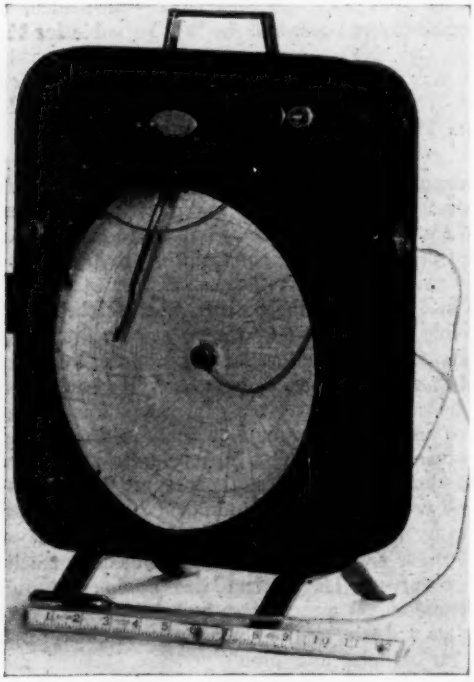

Fig. 1.—The continuous recording thermometer.

From the Department of Surgery, Maimonides Hospital, and New York University College of Medicine, New York.

1. Bigler, J. A., and McQuiston, W. O.: Body Temperatures During Anesthesia in Infants and Children, J. A. M. A. **146**: 551 (June 6) 1951.

2. The thermometer described is manufactured by the Weksler Thermometer Corporation, 52 W. Houston St., New York.

The instrument we have devised (fig. 1 and 2) is an adaptation of a standard industrial, liquid-actuated, clock-motor-driven, recording thermometer.[2] The sensing unit is a specially designed stainless steel bulb on a narrow stem, which can be inserted into the rectum without discomfort to the patient. This is connected to the recording thermometer by a plastic-covered, stainless steel, capillary tube 6 ft. long. Self-contained batteries supply power for electrical contacts set at 103 F and 80 F so that warning lights are switched on automatically at these temperatures. The chart used (fig. 3) has a scale range of 70 to 110 F, which is marked off in 0.5 F divisions and can be read to within 0.25 F. It gives a continuous 12 hour record, with 10 minute and hourly divisions.

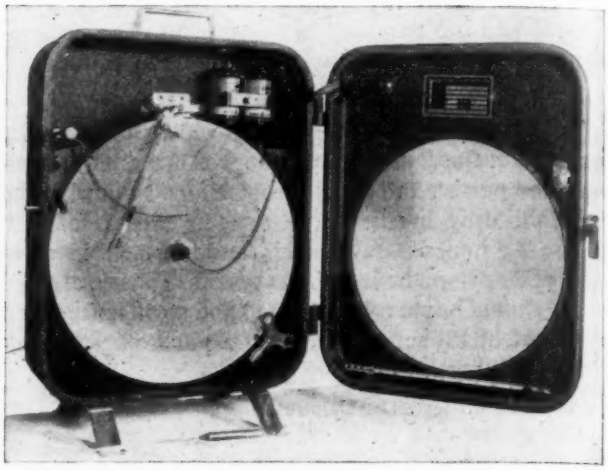

Fig. 2.—Interior of continuous temperature recorder.

For use, the instrument is wound up, the rectal insert is placed in position, and the inked pen is released. The unit requires no attention. Signal lights give warning if the temperature reaches the critical levels of 103 F and 80 F.

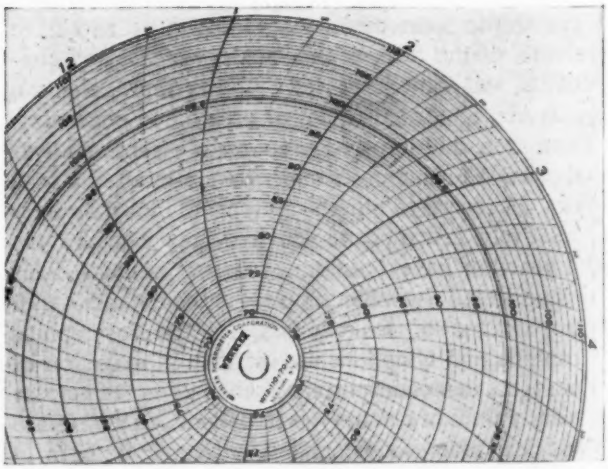

Fig. 3.—Segment of temperature chart, showing time and temperature graduations.

We have used this unit on patients undergoing neurosurgical procedures, patients with pyrexia on a septic basis, and patients being made hypothermic for cardiac surgery. The results have been uniformly satisfactory.

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COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional article has been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Zincasate Burn Dressing.—Zinax Burn Dressing (Hynson, Westcott & Dunning).—Zincasate burn dressing consists of zincasate gel, a partially hydrolyzed casein gel, and zincasate gauze, a zinc acetate impregnated gauze.

Actions and Uses.—Zincasate, a combination of partially hydrolyzed casein gel and zinc acetate impregnated gauze to be applied separately, is used as a dressing for the local treatment of burns by the closed pressure bandage technique. The gel, first applied over the injured area, is converted promptly into an insoluble coagulum at the point of contact with the zinc acetate impregnated gauze to form an adherent, protective, semipermeable membrane that permits the evaporation of water while reducing the loss of transudates. The gel will set eventually without the aid of zinc acetate gauze, so that the layer next to the wound is not immediately coagulated. The gauze, through its union with the adherent gel, provides some pressure and a surface to which an elastic bandage can be applied to increase pressure where this is feasible. The combined use of these materials should follow the same general principle and aseptic technique applicable to the use of petrolatum and plain gauze. The use of a coagulable protein and zinc acetate gauze has the slight advantage of convenience of application, avoidance of maceration, less need for redressing, and production of a pliable protective film permitting easier movement and transport of the patient.

Dosage.—Zincasate gel and gauze dressing are applied after removal of obvious dirt or necrotic tissue, with sterile technique, but without surgical débridement. The casein gel should be applied to superficial as well as to more deeply injured areas to a thickness of not less than ⅛ in. (0.3 cm.) and should extend beyond the borders of such areas. This is then covered with strips of the zinc acetate impregnated gauze, over which a pressure bandage is applied. Alternatively, the gel may be applied to the gauze, which is then placed over the injured area with the gel side in apposition to the wound. In first degree burns or burns that exhibit only erythema the dressing is usually removed the following day. In superficial second degree burns, the dressing may be left intact until healing occurs. At that time the dressing will readily drop away from the wound. Earlier removal can be accomplished by soaking the dressing with warm isotonic sodium chloride solution. In deep second and third degree burns, where grafting may be necessary, the surface is frequently ready for grafting within 9 to 12 days. In such cases it is advantageous to hasten removal of necrotic tissue by redressing once during this period. In severe burns, the gel film separates readily after the dead skin becomes lysed. It is not necessary to use occlusive bandages on the hands, arms, or face or in other areas where this is not feasible. Gauze is applied longitudinally to the extremities, rather than encircling the limb, to avoid abnormal constriction or pressure at vulnerable points. For small or facial burns, the gel and gauze may be applied as a patch without elastic bandage.

Tests and Standards.—

ZINCASATE GAUZE. *Assay:* (Zinc) Transfer to a porcelain crucible an amount of zincasate gauze, accurately weighed, containing the equivalent of about 0.3 gm. of zinc acetate. Add 5 ml. of nitric acid and heat to dryness on a steam bath, and then ignite. Cool the crucible and contents, dissolve the residue in about 5 ml. of diluted hydrochloric acid, filter the solution, and wash both crucible and filter paper with hot water. Bring the clear solution to a volume of about 50-75 ml. and add enough sodium carbonate T.S., dropwise, to precipitate all the zinc as the carbonate. Avoid a large excess of sodium carbonate. Boil the reaction mixture for 5 min., cool, and filter through a tared Gooch crucible. Wash the precipitate thoroughly with hot water until the washings are no longer alkaline. Dry, ignite at 500° for 1 hour, cool, and weigh. Each gram of zinc oxide formed is equivalent to 2.254 gm. of anhydrous zinc acetate. The amount of zinc acetate is not less than 25.0 nor more than 35.0%.

ZINCASATE GEL. *Physical Properties:* Zincasate gel is a pinkish tan viscous liquid with viscosity between 8 x 10^4 and 14 x 10^4 centipoises as determined with the Brookfield viscosimeter. The gel has a pH of 6.5-7.0. It is readily coagulated by zinc acetate.

Purity Tests: Transfer to a tared platinum crucible about 5 gm. of zincasate gel, accurately weighed, and dry at 105° for 10 hours. The amount of residue which remains is not less than 20.0 nor more than 22.0%. Save the residue for the ash determination.

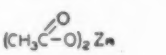
Char the residue from the total solids determination, ignite until all the carbon has been removed, cool, and weigh. The amount of residue is not less than 2.7 nor more than 3.7%.

Assay: (Nitrogen) Transfer to a Kjeldahl flask about 0.1 gm. of zincasate gel and determine the nitrogen by the *U.S.P. semi-micro Kjeldahl method.* Each milliliter of 0.01 *N* acid is equivalent to 0.0001401 gm. of nitrogen. The amount of nitrogen is not less than 2.25 nor more than 2.45%.

(Amino Nitrogen) Transfer to a 250 ml. beaker about 10 gm. of zincasate gel, accurately weighed, add about 75 ml. of water, and stir until solution is complete. Add 10 ml. of neutralized 37% formaldehyde, mix well, and electrometrically titrate the solution with 0.1 *N* sodium hydroxide. Each milliliter of 0.1 *N* sodium hydroxide is equivalent to 0.001401 gm. of nitrogen. The amount of amino nitrogen is not less than 0.18 nor more than 0.20%.

For tests and standards on Zinc Acetate-N.N.R., see the monograph for this material.

Zinc Acetate.—$C_4H_6O_4Zn.2H_2O$.—M.W. 219.50.—The structural formula of zinc acetate may be represented as follows:



Tests and Standards.—

Physical Properties: Zinc acetate is a white, crystalline solid having a pearly luster and a very faint acetic acid odor; upon exposure to air the crystals gradually effloresce. It is freely soluble in water and soluble in alcohol. The pH of a 1% solution is 5.5-7.0.

Identity Tests: Dissolve about 0.1 gm. of zinc acetate in 5 ml. of water, add 0.5 ml. of sulfuric acid, and heat: a strong odor of acetic acid is noticeable *(presence of acetate group).*

Dissolve about 0.1 gm. of zinc acetate in 15 ml. of water and pass hydrogen sulfide through the solution: a white precipitate forms that is insoluble in acetic acid but is soluble in diluted hydrochloric acid *(presence of zinc).*

Purity Tests: Transfer to a 100 ml. volumetric flask 1 gm. of zinc acetate, accurately weighed, add 75 ml. of water, and shake until solution is complete. Add enough ammonium sulfide T.S. to precipitate the zinc completely, fill to the mark with water, mix, and filter. Transfer to a porcelain evaporating dish 50 ml. of the clear filtrate, add 5 drops of sulfuric acid, evaporate to dryness, and ignite to constant weight: the weight of the residue does not exceed 5 mg. *(presence of alkalis and earths).*

Dissolve 0.2 gm. of zinc acetate in 5 ml. of water and run a *U.S.P. arsenic test:* the amount of arsenic does not exceed 10 ppm.

Dissolve 0.5 gm. of zinc acetate in 7 ml. of water and transfer the solution to one of a pair of matched Nessler tubes. Add 10 ml. of 10% potassium cyanide, mix well, and allow the mixture to become clear. Prepare a standard by placing in the other Nessler tube 5 ml. of water, 2.5 ml. of U.S.P. standard lead solution, and 10 ml. of 10% potassium cyanide. To each of the solutions add 0.1 ml. of sodium sulfide T.S., mix the contents, and allow the tubes to stand for 5 min.: the color produced in the sample is not greater than that produced in the standard, indicating not more than 50 ppm of heavy metals.

Assay: (Zinc Acetate) Transfer to a 250 ml. beaker about 1 gm. of zinc acetate, accurately weighed, and add 100 ml. of water. Heat the solution to about 90° and add sodium carbonate T.S., dropwise, to precipitate all of the zinc. Avoid a large excess of sodium carbonate. Boil the mixture for about 5 min. and set it aside to allow the precipitate to settle. Collect the precipitate in a tared Gooch crucible and wash with hot water until the washings are free from alkali. Dry the residue, ignite, and weigh. Each gram of zinc oxide is equivalent to 2.254 gm. of anhydrous zinc acetate. The amount of anhydrous zinc acetate is not less than 82.7 nor more than 87.3%, equivalent to not less than 99.0 nor more than 104.5% of the dihydrate.

Hynson, Westcott & Dunning, Inc., Baltimore, Md.

Zinax Burn Dressing: 8.18 cc. tubes of zincasate gel packaged with 10 gauze pads and 118.3 cc. cans of zincasate gel packaged with 2 yards of gauze. The gauze is impregnated with approximately 30% zinc acetate by weight. U. S. patent 2,579,367.

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POSTGRADUATE CONTINUATION COURSES FOR PHYSICIANS

The semiannual listing of postgraduate continuation courses prepared by the Council on Medical Education and Hospitals appears elsewhere in this issue (page 629). Opportunities for this type of postgraduate education are presented for the six month period beginning July 1. There are a total of 784 courses listed, 418 being offered on a full-time basis and 366 on a part-time schedule. The courses vary in length from a few days to several months. For this six month period, postgraduate education in some form is being given in 37 states, the District of Columbia, and Puerto Rico. The subjects include 34 major areas in the field of clinical medicine and 9 basic science subjects. There are learning opportunities for the physician in general practice as well as the specialist. Many courses are designed to be of assistance to physicians preparing for specialty board certification. The courses available for this purpose are designated by a footnote. A series of courses for military personnel at medical installations is also included. In a number of instances the series of courses for military personnel are made available to civilian physicians. This is also designated by a footnote.

A total of 134 agencies offer postgraduate training in this listing, including 43 medical schools, 35 special medical societies, 18 hospitals, 12 academies of general practice, 11 state medical societies, 6 graduate schools of medicine, and 3 agencies, representing boards of health, schools of public health, and government departments, respectively.

The Council tries to make this listing as complete as possible. Institutions and organizations whose courses are not included in the list are invited to furnish the Council with details pertaining to the opportunities that have been developed for continuation study for physicians.

In addition to the compilation of this semiannual list of postgraduate courses, the Council is engaged in a field study of postgraduate education. A member of the Council's staff has spent the last six months contacting those responsible for such training and collecting facts, figures, and opinions. All sections of the country will have been visited by the summer of 1953. The Council plans to prepare a comprehensive report of its findings.

VIRAL HEPATITIS

The widespread use of blood and blood products during World War II led to the recognition of serum hepatitis as a complication of parenteral injections. In the years that followed, considerable controversy arose as to whether this condition was a disease distinct from infectious (epidemic) hepatitis. In a recent article Stokes [1] has summarized succinctly the evidence favoring the viewpoint that infectious hepatitis (hepatitis A) and serum hepatitis (hepatitis B) are different entities despite their essentially identical clinical manifestations. In his discussion Dr. Stokes draws widely on his own observations of both natural infections and experimentally induced infections in human volunteers.

First, experiments with volunteers and observations under natural conditions have yielded convincing evidence of a lack of cross immunity between the two viruses, thus indicating antigenic differences. Again, Red Cross gamma globulin has been shown repeatedly to give a high degree of protection against infectious hepatitis. On the other hand, with but one known exception, it has proved ineffective against natural or experimentally induced serum hepatitis and in neutralizing virus B. Even gamma globulin prepared from volunteers convalescent from hepatitis A failed to neutralize virus B. Furthermore, convalescent plasma from one such patient failed to neutralize virus B or protect against hepatitis B, thus tending to rule out the possibility that antibodies might be present in a fraction of the globulin other than the gamma fraction.

Another distinguishing feature of the two infections is the presence of the virus in the stools of patients with hepatitis A and the ease with which the disease may be spread by direct contact or by milk, food, or water that contains the virus. On the other hand, Stokes and his associates were unable to produce serum hepatitis by parenteral injection of stool filtrates, which could explain the lack of epidemics of hepatitis B. Again, while the incubation periods of both diseases may be lengthened by low titer or by attenuation of the virus, the mean incubation periods in volunteers and in natural infections will average 20 to 30 days with hepatitis A and 60 to 90 days with hepatitis B. Yet another difference between the two lies in the fact that hepatitis A rarely affects older persons, suggesting that permanent immunity to the disease may develop. There is, however, a high incidence of hepatitis B in older patients, suggesting that this either causes disease infrequently or does not cause complete immunity. The latter view is supported by the fact that in at least five of nine volunteers who had had hepatitis B there were transient mild symptoms

1. Stokes, J., Jr.: Viral Hepatitis, Am. J. M. Sc. **225**: 349, 1953.
2. Neefe, J. R.; Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis: Studies in Volunteers Bearing on Immunological and Other Characteristics of the Etiological Agents, Am. J. Med. **1**: 3, 1946.

and/or laboratory findings suggestive of mild hepatic disturbance when these persons were tested later with the same virus.[2]

Dr. Stokes mentions two other possible differences between hepatitis A and hepatitis B now under active investigation. In the first place, such data as are available suggest that there is a distinctly higher incidence of carriers of hepatitis B than of hepatitis A. In the second place, a skin test for virus A has proved in preliminary tests to be 80 to 95% accurate for detecting persons previously exposed to virus A. In persons known to have had hepatitis B, positive reactions to the test occur in the same percentage as in a random sample of population of the same age range, thus apparently indicating immunity from unrecognized prior infection.

From the evidence presented it appears reasonable to conclude that there is an antigenic distinction between virus hepatitis A and virus hepatitis B and that the differences between the two are apparently greater than mere strain differences, in view of the lack of immunity and of serum antibodies in the older groups of the population to hepatitis virus B. Furthermore, the skin test has provided evidence that hepatitis virus A may be a simple antigenic entity to which one attack gives immunity and for which antibodies remain in the blood during life in appreciable quantities. On the other hand, there is little evidence at present regarding the unity or multiplicity of antigenic types in viral hepatitis B.

WALTER B. MARTIN, M.D.
PRESIDENT-ELECT OF THE AMERICAN MEDICAL ASSOCIATION

REGISTRATION UNDER THE HARRISON NARCOTIC ACT

Physicians who are registered under the Harrison Narcotic Act or under the Marihuana Tax Act must effect reregistration on or before July 1 to avoid a penalty. Each year, despite the annual warnings in THE JOURNAL, this requirement is overlooked by some physicians, and unpleasant consequences follow. Failure to register adds a penalty of 25% to the tax payable and, in addition, subjects the physician to the possibility of a fine not exceeding $2,000 or to imprisonment for a maximum of five years, or to both. The Commissioner of Internal Revenue has in past years given some tardy registrants the choice of paying sums by way of compromise, a procedure authorized by law, or accepting criminal prosecution. If this procedure does not produce the required promptness in reregistration, the commissioner will have no choice but to institute criminal prosecution.

DR. WALTER B. MARTIN— THE PRESIDENT-ELECT

On June 4 Dr. Walter B. Martin of Norfolk, Va., became President-Elect of the American Medical Association. His election by the House of Delegates at its 102nd annual session in New York came in recognition of his many years of outstanding service to the medical profession. In the past 35 years, while conducting an active and successful practice in internal medicine, he has served as member of the Board of Trustees and House of Delegates of the American Medical Association, member of the Association's Council on Medical Service, Committee on Legislation, and Coordinating Committee for the National Educational Campaign against socialized medicine; chairman of a committee for the study of the National Health Service in Great Britain; president of the Norfolk County Medical Society, the Medical Society of Virginia, and the Seaboard Medical Association; vice-president of the Tri-States Medical Association of the Carolinas and Virginia, and member of the Southern Medical Association. During this time he has also rendered distinguished service to the U. S. Army and to his community.

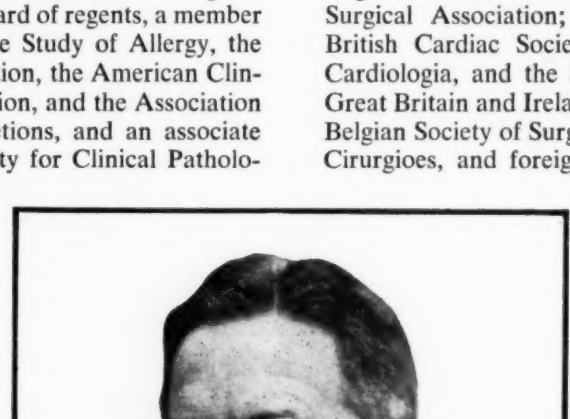
Dr. Martin was born in Pulaski, Va., in 1888. He received a B.S. degree from the Virginia Polytechnic Institute in 1909 and taught chemistry and mathematics at Norfolk Academy from 1910 to 1912. In 1912 he entered Johns Hopkins University School of Medicine and received his M.D. degree in 1916. After completing a year as resident house officer at Johns Hopkins Hospital, he was commissioned lieutenant and then captain in the U. S. Army Medical Corps, where he served as assistant division surgeon, 4th Division, and assistant chief of the medical service at Fort Sheridan General Hospital during World War I. In 1919 he began the practice of internal medicine in Norfolk, Va. There he became chief of the medical service at St. Vincent De Paul Hospital, attending physician in medicine at Norfolk General Hospital, and attending specialist in internal medicine at the U. S. Public Health Service Hospital. From 1942 to 1944 he served as lieutenant colonel in the Army Medical Corps, first at Walter Reed Hospital and then as chief of the

medical service at Percy Jones Hospital, Battle Creek, Mich. In 1944 he became medical consultant to the 5th Service Command and later medical consultant to the 10th Army in the Pacific theater. In 1946, after his discharge from the Army, he was made civilian medical consultant to the Surgeon General of the Army.

Dr. Martin is a diplomate of the American Board of Internal Medicine, a fellow of the American College of Physicians and member of its board of regents, a member of the American Society for the Study of Allergy, the American Rheumatism Association, the American Clinical and Climatological Association, and the Association for the Study of Internal Secretions, and an associate member of the American Society for Clinical Pathologists. He is a member of Phi Beta Kappa, Alpha Omega Alpha, and Nu Sigma Nu fraternities.

DR. ALFRED BLALOCK AWARDED DISTINGUISHED SERVICE MEDAL

At its 102nd annual session in New York, June 1, the House of Delegates of the American Medical Association awarded its highest scientific honor, the Distinguished Service Medal, to Dr. Alfred Blalock of Baltimore for his outstanding work in vascular surgery, especially for his part in the development of the "blue baby operation." This operation, first performed in 1944, has since saved the lives of hundreds of infants with congenital pulmonary stenosis. For this and his many other contributions to surgical science, Dr. Blalock has gained international recognition and an impressive list of honors.



ALFRED BLALOCK, M.D.
AWARDED DISTINGUISHED SERVICE MEDAL

Dr. Blalock was born in 1899 at Culloden, Ga. He received his M.D. degree from Johns Hopkins University in 1922. After serving as intern and resident at Johns Hopkins and at Vanderbilt University Hospital, he became a member of the faculty at the latter institution, where he was active in laboratory and clinical research. In 1940 he published his book "Principles of Surgical Care: Shock and Other Problems" and in the same year was awarded the research medal of the Southern Medical Association for his work on circulatory dynamics in shock. In 1941 he returned to Johns Hopkins University School of Medicine as professor of surgery, director of the department of surgery, and surgeon-in-chief of the Johns Hopkins Hospital. In 1948 he received jointly with Helen Taussig the Passano Foundation Award for the development of the "blue baby operation"; in 1949 he received the René Leriche Award, and in 1950 the Rudolph Matas Award in vascular surgery. The University of Rochester awarded him an honorary doctor of science degree in 1951. In recognition of his work, a number of foreign societies have honored Dr. Blalock. He has been made honorary fellow of the Royal College of Surgeons of England; honorary associate consultant surgeon to Guy's Hospital, London; Chevalier of the Legion of Honor of France; honorary fellow of the Greek Surgical Association; and honorary member of the British Cardiac Society, the Sociedade Brasiliera de Cardiologia, and the Society of Thoracic Surgeons of Great Britain and Ireland. He is a foreign member of the Belgian Society of Surgery and the Colegio Brasiliero de Cirurgioes, and foreign associate of the Académie de Chirurgie of France.

Dr. Blalock's contributions in the field of experimental medicine have earned for him membership in the National Academy of Sciences and the National Research Council. He is also a member of the American Association for the Advancement of Science and the American Society for Clinical Investigation, a consultant on experimental medicine to the Medical Memorial Fund, and a member of the advisory council of the Life Insurance Medical Research Fund. He has been a leader in many national surgical organizations. He is a member of the founders group of the American Board of Surgery and of the Board of Thoracic Surgery, a member of the board of regents of the American College of Surgeons, a past president of the American Association of Thoracic Surgery, and a member of the council of the Southern Surgical Association. He is also a member of the International Society of Surgery, the American Surgical Association, the Society of Clinical Surgery, the Society of University Surgeons, the Society of Vascular Surgery, the Southern Medical Association, and the American Medical Association. In addition Dr. Blalock has rendered valuable service on the editorial boards of a number of medical journals. He has served as associate editor of *Surgery* since 1936; member of the consulting editorial board of *Surgery, Gynecology and Obstetrics* since 1942; member of the editorial board of the *Archives of Surgery* since 1939 and the *American Heart Journal* since 1945; member of the advisory editorial board of the *Journal of Thoracic Surgery* since 1946, and member of the editorial committee of the *American Review of Medicine* since 1948. To these and other journals he has contributed many important original articles on shock, hypertension, heart disease, and other subjects.

MEDICAL NEWS

ARKANSAS

Clinical Assembly.—The Alumni Association of the University of Arkansas School of Medicine, Little Rock, is inaugurating a clinical assembly in conjunction with graduation, June 14-15. Alumni guest speakers will include Drs. James W. McLaurin, Baton Rouge, La.; Horace C. Jones, Grand Rapids, Mich.; and Louis L. Friedman, Birmingham, Ala. A portion of the session will be presented by the medical school faculty. Monday afternoon there will be a symposium on "Recent Trends in Diagnosis and Treatment." The clinical session will be followed by an organization meeting of the alumni association, with Dr. Eugene H. Crawley acting as chairman. All alumni of the University of Arkansas School of Medicine and physicians practicing within the state of Arkansas are cordially invited.

CALIFORNIA

Dr. Pottenger Honored.—At its annual meeting in Atlantic City, N. J., the American College of Physicians bestowed on Dr. Francis M. Pottenger, Monrovia, its highest award, the certificate of "Master." Dr. Pottenger, who has served as president of the Los Angeles County Medical Association, is the author of many papers and books on tuberculosis.

Children's Hospital.—The new $1,500,000 three story Michael J. Connel Clinic was recently dedicated at Childrens Hospital in Los Angeles. It houses 38 clinics capable of serving 350 child outpatients a day.——Children's Hospital has received an $875,475 bequest in the form of a trust fund to be known as the Ernest H. and Dora H. Parker Fund for Medical and Surgical Research.

Society News.—The California Medical Association announces that members who continue to use a method of cancer treatment after being warned that it is valueless will be subjected to censure, suspension, or expulsion from their medical groups. The action followed approval by the association's nine man cancer commission of a 22 page report on the first of a group of products to be evaluated in a full-scale investigation of unproved cancer treatments. The report stated that "no objective evidence was found indicating control of cancer under treatment with this substance alone," and that the product proved "ineffective in three independent studies on laboratory animals." Dr. Ian MacDonald, associate professor of surgery at the University of Southern California School of Medicine, Los Angeles, is chairman of the commission.

COLORADO

Pediatric Clinics in Denver.—The fifth annual summer clinics of the Denver Children's Hospital, which will meet June 24-26 at the hospital, 19th Avenue at Downing Street, will have as guest speakers Drs. Eugene T. McEnery, Chicago, Hattie E. Alexander, New York, and William T. Mustard, Toronto, Canada. The program will include two hour clinics on the diagnosis and treatment of infectious, cardiac, orthopedic, hematological, and chemical disorders in pediatric medicine and surgery. Luncheon, served each day in the hospital, will be followed by a question and answer period. Requests for registration should be addressed to the Chairman of the Summer Clinics, Children's Hospital, Denver 18, together with $5 to apply on the $25 fee.

CONNECTICUT

Fifty Year Club.—The following physicians in the Connecticut State Medical Society were presented with awards and service pins during the annual dinner at the Waverly Inn, Cheshire: Richard F. Rand, Hamden; C. Brewster Brainard, West Hartford; George H. Warner, Bridgeport; Robert Hazen, Thomaston; Frederick B. Bradeen, Essex; and Arthur A. Chase, Plainfield.

Emergency Call Plan.—A full-scale emergency medical call plan to serve residents of New Haven and adjoining communities has been announced by the New Haven Medical Association. The emergency panel comprises 70 physicians in general practice and 88 specialists. Communities covered by the service include East Haven, North Haven, West Haven, Hamden, Branford, Orange, and Woodbridge. The emergency service, organized by a special committee of the association headed by Dr. Samuel Spinner, represents more than four months of surveys and planning, during which questionnaires were mailed to 415 physicians. The New Haven plan is the 15th emergency service to be sponsored by county and local medical associations in Connecticut, thus making emergency medical services available to an estimated 70% of the state's 2 million residents.

FLORIDA

Seminar on Gastroenterology.—Dr. H. Marvin Pollard, professor of internal medicine, University of Michigan Medical School, Ann Arbor, will conduct a seminar on gastroenterology at George Washington Hotel, Jacksonville, June 18-20.

Graduate Short Course.—The 21st annual graduate short course for doctors of medicine will be held at the George Washington Hotel, Jacksonville, June 22-27. The faculty will include Drs. Thomas M. Durant and Julius L. Wilson, Philadelphia, Robert E. Cooke, New Haven, Conn., M. Edward Davis, Chicago, Kenneth W. Warren, Boston, and Conrad G. Collins, New Orleans.

GEORGIA

Fraternity Lectureship.—Phi Delta Epsilon fraternity of the Medical College of Georgia, Augusta, recently presented its annual lectureship, with Dr. Isadore Snapper, Chicago, as guest lecturer, speaking on "Metabolic Bone Diseases."

Narcotic Violation.—Dr. Jarrell M. Estes, Abbeville, was convicted in the U. S. District Court of violating the federal narcotic law and on Jan. 22 was sentenced to serve a term of 24 months.

ILLINOIS

Hospital News.—The Chicago Hospital Council reports that Chicago area hospitals spent nearly 21 million dollars in the last year on construction and improvements. Most of it was used to expand "preventive" medical programs, which sought "to reduce the need for inpatient bed space by improving methods of keeping people healthy before they require hospitalization." At least 12 hospitals installed special flooring and purchased special shoes for operating room personnel to eliminate the danger of explosions caused by static electricity, and 5 general hospitals added or planned for psychiatric units. Chicago area hospitals are reported to have had more than 700,000 outpatient visits during the last fiscal year.——St. Luke's Hospital has opened a campaign to raise $1,500,000 for a medical service building that will consolidate facilities of the hospital and make additional beds available in the present buildings.

Chicago

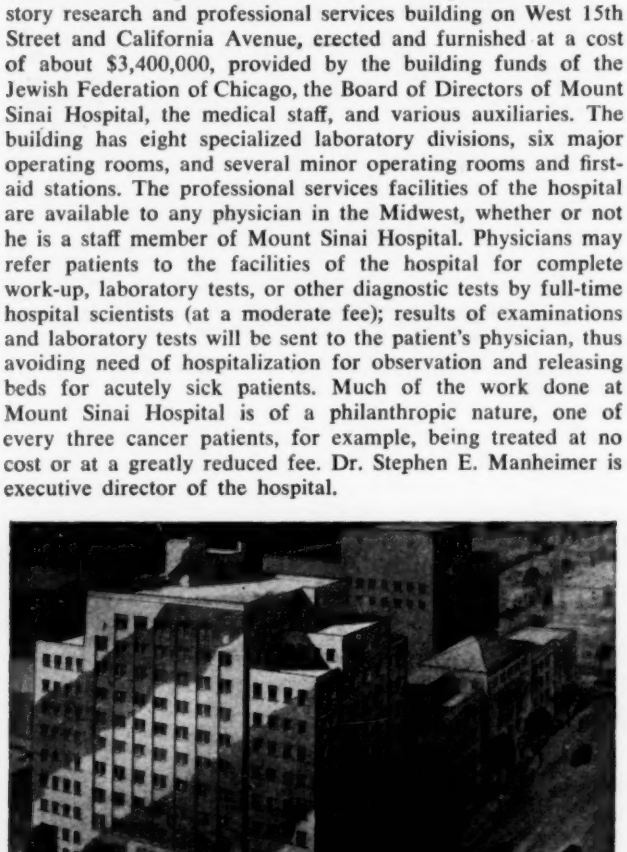
Gift to Medical School.—The Chicago Medical School Faculty Wives Association has presented to the school a check for $8,000, the proceeds of a recent recital sponsored by the association.

Society News.—At its annual meeting the Chicago Society of Internal Medicine elected the following officers: president, Dr. Richard B. Capps, vice-president, Dr. Arthur R. Colwell, Evanston, Ill., and secretary-treasurer, Dr. Edwin N. Irons.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

——At the annual meeting of the Chicago Urological Society the following officers were elected: president, Dr. Andrew McNally, vice-president, Dr. John W. Ferrin, and secretary-treasurer, Dr. Joseph H. Kiefer.

Research-Professional Services Building at Mount Sinai.—Mount Sinai Hospital Medical Center recently dedicated an 11 story research and professional services building on West 15th Street and California Avenue, erected and furnished at a cost of about $3,400,000, provided by the building funds of the Jewish Federation of Chicago, the Board of Directors of Mount Sinai Hospital, the medical staff, and various auxiliaries. The building has eight specialized laboratory divisions, six major operating rooms, and several minor operating rooms and first-aid stations. The professional services facilities of the hospital are available to any physician in the Midwest, whether or not he is a staff member of Mount Sinai Hospital. Physicians may refer patients to the facilities of the hospital for complete work-up, laboratory tests, or other diagnostic tests by full-time hospital scientists (at a moderate fee); results of examinations and laboratory tests will be sent to the patient's physician, thus avoiding need of hospitalization for observation and releasing beds for acutely sick patients. Much of the work done at Mount Sinai Hospital is of a philanthropic nature, one of every three cancer patients, for example, being treated at no cost or at a greatly reduced fee. Dr. Stephen E. Manheimer is executive director of the hospital.



Mount Sinai Research Laboratories and Professional Services Building.

KANSAS

Society News.—The Kansas Psychiatric Society recently elected Dr. William Rottersman, Topeka, president, and Dr. Robert C. Anderson, Topeka, vice-president, and reelected Dr. John R. Adams, Topeka, as secretary-treasurer.

Symposium on Chest Disease.—A symposium on diseases of the chest will be held at the State Sanatorium for Tuberculosis, Norton, 1:30 p. m. June 14, under the auspices of the Northwest Kansas Medical Society. Dr. Carl W. Tempel, Fitzsimons Army Hospital, Denver, will conduct the symposium. Mr. Olaf Soward, Topeka, will speak on "What the Public Thinks of the Medical Profession."

Dr. Thacher Honored.—The town of Waterville recently held a program in honor of Dr. George I. Thacher, who has served nearly 30 years on the board of education, was a commissioner 20 years, and has been mayor. Appointed to the Kansas State Board of Health in 1925, he was elected president of that group in 1936 and served in that capacity for 15 years until his resignation from the board in April, 1951. Dr. Thacher entered the Army as a first lieutenant in 1917, emerged in 1919 with the rank of major, and after World War I rose in the Army reserve to the rank of lieutenant colonel. At 76 he is still active in practice.

MICHIGAN

Meeting of Upper Peninsula Society.—The Upper Peninsula Medical Society will hold its annual meeting June 19-20 in Escanaba. Out-of-state speakers include Drs. John L. Emmett, Rochester, Minn., Leslie W. Freeman, Indianapolis, Robert S. Baldwin, Marshfield, Wis., Lowell D. Snorf, Evanston, Ill., Carl Davis Jr. and Francis E. Senear, Chicago, and Jack A. Klieger and John Steele, Milwaukee.

Personal.—Dr. C. Dale Barrett Jr. has been appointed director of the maternal, child, and school health division of the Detroit Department of Health to succeed Dr. Garner M. Byington, who retired. Dr. Barrett, who came to the department of health in 1949, was previously affiliated with the Ottawa County Health Department, Grand Haven.——Dr. Jerome W. Conn, professor of medicine, University of Michigan Medical School, Ann Arbor, recently delivered the Arthur S. Loevenhart Lecture on "Endocrine Regulation of the Blood Sugar, with Particular Reference to Diabetes Mellitus" for Phi Delta Epsilon of the University of Wisconsin Medical School, Madison.——Dr. William C. Behen, Lansing, has returned after an expedition of about five months, during which he served at eye clinics in Shikarpur, Pakistan, Patna, India, and Barcelona, Spain.

NEW YORK

Dr. Brumfield Appointed to Medical Faculty.—Dr. William A. Brumfield Jr., Albany, first deputy state commissioner of health, has been appointed professor of public health and preventive medicine at State University College of Medicine, Syracuse, where he is expected to assume his new duties about Sept. 1. Dr. Brumfield has been affiliated with Indiana University School of Medicine, Indianapolis, the University of Virginia Hospital, Charlottesville, and, since June, 1935, the New York State Department of Health, returning to it with the rank of colonel after four years in the Army Medical Corps during World War II.

Hospital News.—Dr. Bjorn Vestergaard, Danish psychiatrist, has been appointed to the staff of a special research project in progress at Rockland State Hospital, Orangeburg. His work will be particularly concerned with the relationship of hormones to mental disease. Since October, 1949, Dr. Vestergaard has served as director of biochemical research at Sct. Hans Hospital Ved Roskilde, Denmark, where he conducted biochemical and endocrinological investigations on psychiatric patients. He is the author of scientific papers on this period of his research, published both in Danish and in English.——Dr. Henry S. Martin, immediate past president of the Eighth District Branch of the New York State Medical Society, who has served for nearly 20 years as chief surgeon of the Wyoming County Community Hospital, Warsaw, has been appointed chief of staff emeritus following his resignation from the full-time staff. Dr. George W. Nairn, head of the hospital's eye, ear, nose, and throat department, has been named surgeon-in-chief, and Dr. Paul A. Burgeson will occupy, as acting chief of staff, the other office vacated by Dr. Martin.

New York City

Award to Dr. Papanicolaou.—The Leonard A. Wien Award for Outstanding Research in Cancer Cytology was awarded to Dr. George N. Papanicolaou, professor of anatomy at Cornell University Medical College, during the annual seminar and conference on cancer cytology conducted by the Dade County Cancer Institute in Miami. The award of $1,000, accompanied by a medal, was established by Dr. Leonard A. Wien of Miami, now serving his second year as president of the institute.

Plaque Dedicated to Dr. Munger.—Alumni and faculty of Columbia University's School of Public Health have dedicated a plaque in the school library at the Columbia-Presbyterian Medical Center to the late Dr. Claude W. Munger, professor of hospital administration at the school, 1945-1950. Among the speakers were Dr. Harry S. Mustard, former New York City Health Commissioner, and Dr. E. Dwight Barnett, director

of the Institute of Administrative Medicine, Columbia University. Dr. Munger, who died in 1950, in addition to his teaching duties as a member of the faculty of Columbia University College of Physicians and Surgeons was director of St. Luke's Hospital for 11 years and president of the American Hospital Association in 1936 and 1937.

Personal.—On their recent tour, Dr. Ralph Colp, clinical professor of surgery, and Dr. William M. Hitzig, assistant clinical professor of medicine, Columbia University College of Physicians and Surgeons, lectured and made rounds at the General Hospital of the University of Malaya Medical School. Dr. Colp spoke on "Recent Methods in the Surgical Management of Gastric and Duodenal Ulcer," and Dr. Hitzig on "Medicine at the Crossroads." Both men were guests at Singapore of Mr. Mekie, professor of surgery, and Prof. Ransome, professor of medicine, University of Malaya Medical School. Drs. Colp and Hitzig made observations on police medicine, as part of a far eastern survey that took them to China, Thailand, Cambodia, Viet-Nam, and India before their departure for England.

NORTH CAROLINA

Postgraduate Course at Durham.—The Duke University School of Medicine, Durham, offers a postgraduate course June 22-25 at Duke Hospital (registration fee, $25). Monday and Tuesday will be devoted to anesthesia, with round-table discussions at 8 p. m. The Wednesday program will include liver diseases, allergic diseases, and intravenous alimentation, and on Thursday neoplasms and head injuries will be discussed. Ward rounds and clinic visits will be held Wednesday and Thursday. Guest lecturers will be Drs. Howard M. Ausherman, chief of anesthesia, VA Hospital, Durham, and David A. Davis, professor of anesthesiology, University of North Carolina School of Medicine, Chapel Hill. Other lecturers will be from the staff of Duke University School of Medicine. The faculty of the medical school will give a barbecue for all participants of the course Wednesday, 6:30 p. m. For information, address Director of Postgraduate Education, Box 3088, Duke Hospital, Durham.

NORTH DAKOTA

Clinic Observes Silver Anniversary.—The 25th anniversary of the Northwest Clinic, Minot, was recently observed, with (1) an open house reception for the public; (2) a program on which Dr. Edwin F. Hirsch, pathologist of St. Luke's Hospital, Chicago, discussed "Cancer of the Lungs"; and (3) a dinner in the Clarence Parker Hotel at which Dr. Russell A. Nelson, director of the Johns Hopkins Hospital, Baltimore, was guest speaker.

OHIO

Golfers' Tournament.—The Ohio State Medical Golfers' Association will hold its annual tournament June 18 at the Elyria Country Club (on U. S. 20 between Elyria and Oberlin). Any male physician who is a member in good standing of the Ohio State Medical Association may send an application to Bob Elwell, Secretary and Treasurer, Ohio State Medical Golfers' Association, 3101 Collingwood Blvd., Toledo 10. The initiation fee for new members is $5, and the greens fee, luncheon, banquet, and prizes, $14.

RHODE ISLAND

Brown University Appoints Health Director.—Dr. Charles J. Hutchinson, recently retired chief medical officer of the Boston Naval Shipyard, former professor at the University of Minnesota School of Medicine, Minneapolis, has been appointed full-time director of the Brown University Health Division, to succeed Dr. Charles A. McDonald, who will reach the retirement age July 1. His duties will include supervision of the health services for Brown and Pembroke undergraduates and students of the graduate school. Following World War I duty, Dr. Hutchinson held naval reserve status and in 1940 was recalled to active duty when he took charge of the naval dispensary at the University of Minnesota. Thereafter, he was engaged in the medical outfitting of ships on the Pacific Coast and served for a time as senior medical officer of an attack transport whose mission was the evacuation of casualties from Pacific island invasion beaches.

SOUTH DAKOTA

State Medical Meeting at Rapid City.—The South Dakota State Medical Association will hold its annual meeting in the City Auditorium, Rapid City, June 14-16. Dr. Roy E. Jernstrom, Rapid City, will deliver the presidential address at the annual banquet in the Alex Johnson Hotel June 15 at 7 p. m. Alfred P. Haake, Ph.D., Chicago, economic consultant to General Motors Corporation, will be guest speaker at the banquet, which will be preceded by open house at the Rapid City Medical Center, 5-7 p. m. The first general session will open Monday, 8:15 a. m., with a film on "Dermatologic Procedures for the General Practitioner." The following topics will be discussed by guest speakers:

Artificial Kidney, Oliver G. Stonington, Denver.
Problems of the Newborn, Paul D. Bruns, Denver.
Surgery of Stenotic Valvular Heart Disease with Emphasis on Congenital Malformations, Robert P. Glover, Philadelphia.
Rheumatoid Spondylitis—Its Diagnosis and Treatment, Charley J. Smyth, Denver.
Treatment of Common Eye Diseases and Management of Eye Injuries, Robert W. Hollenhorst, Rochester, Minn.
Points to Remember When Treating Severe Epistaxis, Olav E. Hallberg, Rochester, Minn.
Common Pitfalls of Fracture Treatment, Roger Anderson, Seattle.
Cutaneous Malignancies—Common and Uncommon, Henry M. Lewis, Denver.
Surgery of the Biliary Tract, Howard K. Gray, Rochester, Minn.
Applied Psychiatry in General Practice, Franklin G. Ebaugh, Colorado.
Health Education, William W. Bolton, Chicago.

The Woman's Auxiliary to the South Dakota State Medical Association will meet simultaneously in Rapid City. The national auxiliary vice-president, Mrs. George Turner, El Paso, Texas, will address the state medical meeting Monday, 9:40 a. m., on "Auxiliary Role in Medicine."

The program of the South Dakota Academy of Ophthalmology and Otolaryngology, Monday, will be presented by Drs. Hollenhorst and Hallberg, Rochester, Minn.

WEST VIRGINIA

Postgraduate Session.—The annual postgraduate session sponsored by the Barbour-Randolph-Tucker Medical Society will be held at the Tygart Valley Country Club, near Elkins, June 18. The morning will be devoted to golf. The following program will be presented at 2 p. m.:

James B. Arey, Philadelphia, Pathological Basis for Respiratory Disturbances in the Newborn.
Louis K. Alpert, Washington, D. C., Collagen Disorders.
James G. Arnold Jr., Baltimore, Low Back Pain.
J. Edwin Wood Jr., Charlottesville, Management of Congestive Heart Failure.

Dr. Guy H. Michael, Parsons, will serve as moderator. A question and answer period will follow the presentation of each paper. A social hour is planned for 5:30 p. m., with the Kloman Instrument Company of Charleston as the host. Dr. Louis A. M. Krause, professor of clinical medicine, University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, will address the annual banquet at 6:30 p. m. on "Medicine and the Bible." The Barbour-Randolph-Tucker Medical Society, of which Dr. Louis H. Nefflen, Elkins, is president, has extended a cordial invitation to all members of the West Virginia State Medical Association to attend the meeting.

GENERAL

Meeting of Physical Therapists.—The annual conference of the American Physical Therapy Association will be held at the Baker Hotel, Dallas, Texas, June 15-19. The theme for the program will be "The Patient—His Evaluation and Program for Rehabilitation."

Myasthenia Gravis Meeting.—The Medical Board of the Myasthenia Gravis Foundation, Inc. (480 Lexington Ave., New York 17), under the chairmanship of Dr. Henry R. Viets, Boston, will hold its first meeting in Atlantic City on the evening of June 14. The meeting will be preceded by a reception and dinner at the Hotel Claridge.

Conference on Growth.—The Society for the Study of Development and Growth has received a grant of $1,500 from the National Science Foundation in partial support of a symposium on specificity in development to be held at the University of New Hampshire, Durham, June 19-22. The American Cancer Society, the National Cancer Institute, and the National Research Council are also supporting the symposium. The conference will include discussions of such subjects as the manufacture of proteins in the body, the part played by enzymes in development of cells and organs, and the influence of hormones on development of the embryo. The meetings will be open to all interested scientists.

United Cerebral Palsy Appoints Medical Director.—Dr. Glidden L. Brooks, associate professor of pediatrics, University of Pittsburgh School of Medicine, has been appointed the first full-time medical director of United Cerebral Palsy, for which he has been serving as medical consultant. He was formerly affiliated with the Harvard Medical School and the Children's Medical Center in Boston, Central Maine General Hospital in Lewiston, and University of Pennsylvania School of Medicine and Children's Hospital in Philadelphia. In Pittsburgh he has been coordinator of hospitals and clinics at the University of Pittsburgh, professor of hospital administration in the Graduate School of Public Health, associate physician to the Children's Hospital, and consultant in charge of pediatrics at Montefiore Hospital.

Society News.—The Southwest Allergy Forum will meet at the Hotel Muehlebach, Kansas City, Mo., June 14-16 under the presidency of Dr. Orval R. Withers of that city. The sessions will be devoted primarily to papers on practical aspects of allergy.——Dr. Randall G. Sprague, associate professor of medicine at the Mayo Foundation and consulting physician at the Mayo Clinic, Rochester, Minn., a diabetic since childhood, was elected president of the American Diabetes Association at its annual meeting in New York City. Dr. Sprague, the first diabetic to hold this office, addressed a free public meeting open to diabetics, their families, and friends, on "The Art of Living with Diabetes," in which he described his 30 years' experience as a diabetic, as a physician treating diabetics, and as a scientist studying diabetes.

Neurologists Meet in Atlantic City.—The American Neurological Association will hold its annual meeting June 15-17 at the Hotel Claridge, Atlantic City, N. J. Dr. Hans H. F. Reese, Madison, Wis., will deliver the presidential address Monday at 9 a. m. At 8 p. m. the following symposium on neurological education will be held in Trimble Hall:

Philosophy of a Medical School Department of Neurology, Roland P. Mackay, Chicago.
Content of the Neurological Course, Russell N. De Jong, Ann Arbor, Mich.
Techniques, Adolph L. Sahs, Iowa City.
Organization of a Neurological Department in a Medical School, H. Houston Merritt, New York.
Graduate and Postgraduate Training, Henry W. F. Woltman, Rochester, Minn.

The Tuesday morning session will be devoted to 10 presentations with moving picture demonstrations (board room), including results of electroencephalograms, pneumoencephalograms, carotid angiography, and attempts at dural sinus visualization in the case of the Brodie craniopagus twins. The annual dinner for members of the association and guests will be held Tuesday, 7 p. m. The American Association of Neuropathologists will hold its meeting Sunday, June 14, at the Hotel Claridge.

Medical Librarians Meet in Salt Lake City.—The annual meeting of the Medical Library Association, Inc., will be held at the Newhouse Hotel, Salt Lake City, June 16-19. At the opening session Tuesday 2 p. m. Drs. John Z. Bowers, dean, University of Utah College of Medicine, and Kenneth B. Castleton, president, Utah State Medical Association, will welcome the delegates. "Methods of Investigation of Human Inheritance" will be discussed by Dr. Frank H. Tyler and Fayette E. Stephens, Ph.D., University of Utah. The medical school group will meet at 8 p. m. in the Franciscan Room. "Medical School Library Administration" will be discussed by Frank A. Lundry, M.A., director of libraries, University of Nebraska, and "The Role of the Medical Library in the Medical School Curriculum" by Chauncey D. Leake, Ph.D., vice-president, University of Texas Medical Branch, Galveston. On Wednesday at 3:30 p. m. Dr. Ralph T. Richards, Salt Lake City, will present "The Development of Medicine in Utah." The annual banquet will be held in the Bonneville Room at 7 p. m. Dr. C. H. Hardin Branch, University of Utah College of Medicine, will be the speaker at luncheon Thursday, 12:30 p. m. in the University of Utah Union Building ballroom. At 2:15 p. m. a film, "Seizure," will be shown in the theater of the VA Hospital, Fort Douglas. Introduction and comments will be made by Dr. Madison H. Thomas, University of Utah. Dr. Sanford V. Larkey, Baltimore, chairman, American Documentation Institute, will participate in the general session on national and international activities Friday, 9 a. m., in the Gold Ballroom.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions in the weeks ended as indicated:

Area	May 30, 1953 PAR	NP	NS	May 24, 1952, Total
United States	61	54	83	145
New England States				
Maine	1	..	..	2
New Hampshire	..	..	..	..
Vermont	..	..	..	..
Massachusetts	2	1	1	1
Rhode Island	..	..	..	..
Connecticut	..	..	1	..
Middle Atlantic States				
New York	4	..	7	4
New Jersey	1	..	..	1
Pennsylvania	..	..	1	2
East North Central States				
Ohio	1	..	1	..
Indiana	..	..	5	..
Illinois	..	..	2	8
Michigan	1	5	1	..
Wisconsin	..	..	2	2
West North Central States				
Minnesota	3	..	2	2
Iowa	..	3	..	1
Missouri	3	2	..	2
North Dakota	..	..	..	..
South Dakota	..	..	1	..
Nebraska	2	1	..	1
Kansas	..	..	..	2
South Atlantic States				
Delaware	..	..	..	1
Maryland	1	..	..	..
District of Columbia	..	..	1	..
Virginia	4	..	..	..
West Virginia	1	2	1	2
North Carolina	1	1	..	1
South Carolina	..	..	..	1
Georgia	..	..	1	2
Florida	2	..	3	4
East South Central States				
Kentucky	3	..	..	1
Tennessee	..	2	5	2
Alabama	..	..	11	..
Mississippi	..	..	4	5
West South Central States				
Arkansas	2	..	..	1
Louisiana	2	3	..	3
Oklahoma	..	1	2	7
Texas	13	13	21	47
Mountain States				
Montana	..	..	..	..
Idaho	..	..	..	4
Wyoming	..	..	..	..
Colorado	..	..	4	1
New Mexico	..	..	..	..
Arizona	2	..	1	4
Utah	..	..	2	..
Nevada	..	..	..	..
Pacific States				
Washington	..	..	..	5
Oregon	2	..	..	2
California	10	20	3	24
Territories and Possessions				
Alaska	..	..	..	..
Hawaii	..	..	1	3
Puerto Rico	1	..	..	..

PAR = paralytic; NP = nonparalytic; NS = type not stated.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1953 Clinical Session, St. Louis, Dec. 1-4.

1954 Annual Session, San Francisco, June 21-25.

1954 Clinical Session, Miami, Florida, Nov. 30-Dec. 3.

1955 Annual Session, Atlantic City, N. J., June 6-10.

ALASKA TERRITORIAL MEDICAL ASSOCIATION, Sitka, July 15-17. Dr. William P. Blanton, P. O. Box 2569, Juneau, Secretary.

AMERICAN GYNECOLOGICAL SOCIETY, Lake Placid Club, Lake Placid, N. Y., June 15-17. Dr. John I. Brewer, 104 South Michigan Ave., Chicago, Secretary.

AMERICAN NEUROLOGICAL ASSOCIATION, Hotel Claridge, Atlantic City, N. J., June 15-17. Dr. H. Houston Merritt, 710 West 168th St., New York 32, Secretary.

AMERICAN ORTHOPEDIC ASSOCIATION, The Homestead, Hot Springs, Va., June 20-July 1. Dr. George O. Eaton, 4 East Madison St., Baltimore 2, Secretary.

AMERICAN VETERINARY MEDICAL ASSOCIATION, Royal York Hotel, Toronto, Canada, July 20-23. Dr. J. G. Hardenbergh, 600 South Michigan Blvd., Chicago 5, Executive Secretary.

IDAHO STATE MEDICAL ASSOCIATION, Sun Valley, June 14-17. Dr. Robert S. McKean, 305 Sun Bldg., Boise, Secretary.

MAINE MEDICAL ASSOCIATION, Eastland Hotel, Portland, June 21-24. Mr. W. Mayo Payson, 142 High St., Portland 3, Executive Secretary.

MEDICAL LIBRARY ASSOCIATION, New House Hotel, Salt Lake City, June 16-19 Miss Louise C. Lage, Lilly Research Laboratories, 740 South Alabama St., Indianapolis 6, Secretary.

PACIFIC DERMATOLOGIC ASSOCIATION, Olympic Hotel and University of Washington, Seattle, July 9-10. Dr. Ervin H. Epstein, 447 29th St., Oakland 9, Calif., Secretary.

ROCKY MOUNTAIN CANCER CONFERENCE, Denver, July 8-9. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Secretary.

SOUTH DAKOTA STATE MEDICAL ASSOCIATION, Alex Johnson Hotel, Rapid City, June 14-16. Dr. G. I. W. Cottam, 300 First National Bank Bldg., Sioux Falls, Secretary.

SOUTHWEST ALLERGY FORUM, Hotel Muehlebach, Kansas City, Mo., June 14-16. Dr. Frederic Speer, 2601 Parallel Ave., Kansas City 4, Kans., Secretary.

STUDENT AMERICAN MEDICAL ASSOCIATION, Edgewater Beach Hotel, Chicago, June 15-17. Mr. Russell F. Staudacher, 535 North Dearborn St., Chicago 10, Executive Secretary.

UPPER PENINSULA MEDICAL SOCIETY, Escanaba, Mich., June 19-20. Dr. N. L. Lindquist, 1103 Ludington St., Escanaba, Mich., Secretary.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, The Greenbrier, White Sulphur Springs, July 23-25. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

FOREIGN

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, Leeds, England, May 13-15, 1954. Dr. Henry W. S. Wright, 45 Lincoln's Inn Fields, London W.C.2, England, Honorary Secretary.

BRITISH MEDICAL ASSOCIATION, Cardiff, S. Wales, July 13-17. Dr. A. MaCrae, B. M. A. House, Tavistock Square, London W.C.1, England, Secretary.

CANADIAN MEDICAL ASSOCIATION, Winnipeg, Manitoba, Canada, June 15-19. Dr. T. C. Routley, 135 St. Clair Avenue W., Toronto 5, Ontario, Canada, General Secretary.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Chateau Frontenac, Quebec, Canada, October 26-29. Dr. A. William Friend, 515 Nome Ave., Akron 20, Ohio, Chairman, Program Committee.

CONGRESS OF INTERNATIONAL LEAGUE AGAINST RHEUMATISM, Geneva and Zurich, Switzerland, Aug. 24-29. For information write: Dr. W. Tegner, The London Hospital, London E.1, England.

CONGRESS OF THE INTERNATIONAL SOCIETY OF ANGIOLOGY, Lisbon, Portugal, Sept. 18-20. Dr. Henry Haimovici, 105 East 90th St., New York 28, N. Y., U. S. A., Secretary.

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 14-20. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 15-19, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS OF ACUPUNCTURE, Kolpinghaus, Adolf-Kolping-Strasse 1, Munich, Germany, August 22-25. Dr. G. Bachmann, 29 Lilienstrasse, München 9, Germany, Organizer and Secretary.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF THE EUROPEAN SOCIETY OF HAEMATOLOGY, Amsterdam, Holland, Sept. 8-12. Dr. M. C. Verloop, Maliesingle 15, Utrecht, Holland, Secretary.

INTERNATIONAL CONGRESS ON GENETICS, Bellagio, Italy, August 24-31. Prof. C. Barigozzi, Instituto de Genetica, Universita de Milano, 10 via Celoria, Milan, Italy, Secretary.

INTERNATIONAL CONGRESS OF HIPPOCRATIC MEDICINE, Evian, France, Sept. 3-6. Prof. P. Delore, 13 rue Jarente, Lyons, France, Secretary-General.

INTERNATIONAL CONGRESS FOR HISTORY OF SCIENCE, Jerusalem, Israel, August 3-7. Prof. F. S. Bodenheimer, Hebrew University, Jerusalem, Israel, President.

INTERNATIONAL CONGRESS OF HYDROCLIMATISM AND THALASSOTHERAPY, Dubrovnik, Yugoslavia, May 8-16, 1954. Prof. C. Plavsic, Zeleni Venac 1, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Sao Paulo, Brazil, April 26-May 2, 1954. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U.S.A., Secretary-General.

INTERNATIONAL CONGRESS OF LOGOPEDICS AND PHONIATRICS, Milan and Stresa, Italy, Sept 1-7. Dr. Deso A. Weiss, 115 East 86th St., New York 28, N. Y., U. S. A., General Secretary.

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP, London, England, July 20-25. Mr. W. R. LeFanu, % London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, England, Chairman.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept 6-12. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS ON OBSTETRICS AND GYNECOLOGY, Geneva, Switzerland, July 26-31, 1954. Dr. H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland, President.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Havana, Cuba, Oct. 12-17. Prof. Felix Hurtado, 5a Avenue 124, Miramar, Havana, Cuba, President.

INTERNATIONAL CONGRESS OF RADIOLOGY, Copenhagen, Denmark, July 19-25. Professor Flemming Norgaard, 10 Oster Voldgade, Copenhagen K, Denmark, Secretary General.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyoglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL CONVENTION OF X-RAY TECHNICIANS, Royal York Hotel, Toronto, Canada, June 28-July 2. For information write: Miss Beatrice Hurley, R.T., Registrar, St. Catherine Hospital, East Chicago, Ind., U. S. A.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL LEPROSY CONGRESS, Madrid, Spain, Oct. 3-10. Dr. Felix Contreras, Moreto 15, Madrid, Spain, Secretary.

INTERNATIONAL NEUROLOGICAL CONGRESS, LISBON, Portugal, Sept. 7-12. Prof. Almeida Lima, Avenida do Brazil 53, Lisbon, Portugal, Secretary-General.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL PSYCHO-ANALYTICAL CONGRESS, Bedford College, Regent's Park, London N.W.1, England, July 26-30. Dr. Ruth S. Eissler, 285 Central Park West, New York 24, N. Y., Hon. Secretary.

INTERNATIONAL SOCIETY FOR THE STUDY OF BIOLOGICAL RHYTHMS, Basle, Switzerland, Sept. 18-19. For information write: Prof. Dr. F. Georgi, Neurologische Universitats-Poliklinik, Socinstrasse 55, Basle, Switzerland.

INTERNATIONAL VETERINARY CONGRESS, Stockholm, Sweden, Aug. 9-15. Prof. Axel Isaksson, Institute of Veterinary Medicine, Stockholm 50, Sweden, Secretary.

IRISH MEDICAL ASSOCIATION, Waterford, Ireland, July 1-4. Dr. P. J. Delaney, 10, Fitzwilliam Place, Dublin, Ireland, Medical Secretary.

LATIN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY, Caracas, Venezuela, Feb. 21-25, 1954. Dr. Victorino Marquez Reveron, Centro Medico, Caracas, Venezuela, Secretary-General.

PACIFIC SCIENCE CONGRESS, Quezon City and Manila, Philippines, Nov. 16-28. Dr. Patrocinio Valenzuela, College of Pharmacy, University of the Philippines, Quezon City, Philippines, Secretary-General.

PAN AMERICAN CONGRESS OF THE MEDICAL PRESS, Buenos Aires, Argentine, July 12-16. Secretaria del Congress, 763 Uriburu, Buenos Aires, Argentine.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, Mexico, D.F., Mexico, Feb. 28-March 4, 1954.

SECTIONAL MEETING, AMERICAN COLLEGE OF SURGEONS, London, England, May 17-19, 1954. Dr. Michael L. Mason, 40 East Erie St., Chicago 11, Ill., U. S. A., Secretary.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 22-29. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICAL THERAPY, London, England, Sept. 7-12. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C.1, England, Secretary.

WORLD MEDICAL ASSOCIATION, The Hague, Netherlands, Aug. 31-Sept. 7. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary-General.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 23-25. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery.

ARKANSAS:* *Regular. Examination.* Little Rock, June 18-19. Sec., Dr. Joe Verser, Harrisburg. *Homeopathic. Examination.* Little Rock, April 6. Sec., Dr. Carl S. Bungart, 105 North 14th St., Ft. Smith. *Eclectic.* Little Rock, June 4-5. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

CALIFORNIA: San Francisco, June 22-25. Asst. Sec., Mr. Wallace D. Thompson, 1020 N Street, Sacramento 14.

COLORADO:* *Reciprocity.* Denver, July 14. Final date for filing applications is June 12. Exec. Sec., Mrs. B. H. Hudgens, 831 Republic Bldg., Denver. 2.

CONNECTICUT:* *Regular. Examination.* Hartford, July 14-15. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven. *Homeopathic.* Derby, July 14-15. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: Dover, July 14-16. Sec., Dr. Joseph S. McDaniel, 229 South State St., Dover.

FLORIDA:* Jacksonville, June 28-30. Sec., Dr. Homer Pearson, 701 Dupont Bldg., Miami.

GEORGIA: *Examination.* Atlanta and Augusta, June 9-10. *Reciprocity.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

HAWAII: *Examination.* Honolulu, July 13-15. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, July 13-15. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: Chicago, July 7-9. Supt. of Regis., Mr. Fredric B. Selcke, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June 23-25. Ex. Sec., Miss Ruth V. Kirk, 538 K of P Bldg., Indianapolis.

IOWA:* *Examination.* Iowa City, June 15-17. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 10-11. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 8-10. Sec., Dr. Bruce Underwood, 620 South Third St., Louisville 2.

MAINE: *Reciprocity and Examination.* Augusta, July 14-15. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, June 16-19. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, July 14-17. Sec., Dr. Robert C. Cochrane, Room 37, State House, Boston 33.

MICHIGAN: *Examination.* June 10-12, Ann Arbor and Detroit. Sec., Dr. J. Earl McIntyre, 201-4 Hollister Bldg., Lansing.

MINNESOTA:* *Reciprocity.* St. Paul, May 22-23. *Examination.* St. Paul, June 16-18. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul.

MISSISSIPPI: Jackson, June 22-24. Sec., Dr. Felix J. Underwood, Old Capitol Bldg., Jackson 113.

MONTANA: Helena, Oct 5. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA:* *Examination.* Omaha, June 15-17. Director, Mr. Husted K. Watson, Room 1009 State Capitol Bldg., Lincoln 9.

NEW HAMPSHIRE: Concord, Sept. 9. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: Trenton, June 16-19. Sec., Dr. Earl S. Hallinger, 28 West State St., Trenton.

NEW MEXICO:* Oct. 12-13, Santa Fe. Sec., R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, June 23-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany 7.

NORTH CAROLINA: *Examination.* Raleigh, June 22-25. *Reciprocity.* Raleigh, June 23. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: Grand Forks, July 8-11. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, June 15-17. *Reciprocity.* Columbus, July 7. Sec., Dr. H. M. Platter, 21 W. Broad, Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 10-11. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, July 9-10. *Reciprocity.* Portland, July 24. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July. Act. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* Providence, July 2-3. Administrator of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 22-24. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* Rapid City, June 17-18. Exec. Sec., Mr. John C. Foster, 300 1st National Bank Bldg., Sioux Falls.

TENNESSEE:* Nashville, June 10-11. Memphis, June 17-18. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS:* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Ft. Worth 2.

UTAH: *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City.

VERMONT: Burlington, June 15-17. Sec., Dr. F. J. Lawliss, Richford.

VIRGIN ISLANDS: *Examination.* St. Thomas, June 10-11. Sec., Dr. Earle M. Rice, Box 8, St. Thomas.

VIRGINIA: *Examination and Reciprocity.* Richmond, June 17-20. Address: Secretary, Board of Medical Examiners, 631 First St. S.W., Roanoke.

WASHINGTON:* Seattle, July 12-15. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WEST VIRGINIA: Charleston, July 13-15. Sec., Dr. N. H. Dyer, State Office Bldg., Charleston 5.

WISCONSIN:* *Examination.* Milwaukee, July 14-16. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

WYOMING: *Oral. Reciprocity.* Cheyenne, June 8. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

PUERTO RICO: *Reciprocity.* Santurce, Aug. 4. Sec., Mr. Luis Cueto Coll, Box 9156, Santurce.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARIZONA: Tucson, June 16. Sec., Mr. Herbert D. Rhodes, University of Arizona, Tucson.

COLORADO: *Examination.* Denver, Sept. 9-10. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

CONNECTICUT: *Examination.* New Haven, June 13. Exec. Asst., Miss M. G. Reynolds, 110 Whitney Ave., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, Oct. 19-20. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

IOWA: Des Moines, July 14. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

NEVADA: Reno, July 7. Sec., Mr. Frank Richardson, University of Nevada, Reno.

NEW MEXICO: Santa Fe, June 21. Sec., Mrs. Marguerite Cantrell, P. O. Box 1592, Santa Fe.

TENNESSEE: Memphis, July 2-3. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

TEXAS: *Examination.* Austin, October. Chief Clerk, Mrs. Sandra Allen, 407 Perry-Brooks Bldg., Austin.

WASHINGTON: *Examination.* Seattle, July 8-9. Sec., Department of Licenses, Mr. Edward C. Dohm, Olympia.

WISCONSIN: *Examination.* Milwaukee, June 13. Final date for filing application is June 6. Madison, Sept. 19. Final date for filing application is Sept. 11. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

* Basic Science Certificate required.

DEATHS

Longcope, Warfield Theobald ⊕ Lee, Mass., professor emeritus of medicine at his alma mater, died at his home on Cornhill Farm April 25, aged 76, of emphysema. Dr. Longcope was born in Baltimore March 29, 1877, and received his M.D. degree from Johns Hopkins University School of Medicine in Baltimore in 1901. He then spent 10 years in Philadelphia, as resident pathologist of the Pennsylvania Hospital, 1901-1904, as director of the Ayer Clinical Laboratory, 1904-1911, and as assistant professor of applied medicine at the University of Pennsylvania School of Medicine from 1909 to 1911. In the autumn of 1911 Dr. Longcope moved to New York and during the next 10 years filled important positions at Columbia University and the Presbyterian Hospital simultaneously. He was an associate professor, 1911-1914, Bard Professor of Applied Medicine 1914-1921 at Columbia, and during the same period an associate visiting physician, then director of medical service at the Presbyterian Hospital. In 1934 he was elected a member of the board of scientific directors of the Rockefeller Institute for Medical Research in New York City and in 1939 was elected president. In 1922 he became professor of medicine at Johns Hopkins University School of Medicine in Baltimore and retired in June, 1946, after 24 years' affiliation with the institution. For a short time in 1922 he was a professor of clinical medicine at Cornell University Medical College in New York. During World War I he served in the medical division of the Office of the Surgeon General and with the American Expeditionary Forces. He was a specialist certified by the American Board of Internal Medicine, an Associate Fellow of the American Medical Association, formerly vice-president and president of the Association of American Physicians, which in 1948 awarded him the George M. Kober medal for his contribution to medicine and medical education, and formerly vice-president of the American Association for the Advancement of Science. He was a member of the American Society for Clinical Investigation, American Clinical and Climatological Association, National Academy of Sciences, American Society for Experimental Pathology, New York Academy of Medicine, American Academy of Arts and Sciences, and the Harvey Society; fellow of the American College of Physicians, an honorary member of the Societé des Hôpital aux de Paris, and Royal Society of Medicine; and an honorary fellow of the Scandinavian Congress for Internal Medicine and the College of Physicians of Philadelphia. In 1934 Dr. Longcope received the honorary degree of doctor of laws from St. John's College in Annapolis, Md., in 1941 the degree of doctor of science from the University of Rochester in Rochester, N. Y., and in 1945 the Docteur "honoris causa," University of Paris. Dr. Longcope's own extensive researches were conducted in the fields of clinical medicine and pathology.

Gray, Irving ⊕ Brooklyn; born in New York City in 1892; University and Bellevue Hospital Medical College, New York, 1913; specialist certified by the American Board of Internal Medicine; member of the American Gastro-Enterological Association, American Public Health Association, and the Industrial Medical Association; fellow of the American College of Physicians; during World War I served in the medical corps; consulting physician, Brooklyn State and Coney Island hospitals in Brooklyn, Sea View Hospital in Staten Island, St. Joseph Hospital in Far Rockaway, Long Beach (N. Y.) Memorial Hospital, and Rockaway Beach (N. Y.) Hospital; died April 21, aged 60.

Howles, James Kirby ⊕ New Orleans; born in Memphis, Tenn., Jan. 5, 1898; University of Cincinnati College of Medicine, 1929; professor of dermatology and syphilology and head of the department of Louisiana State University School of Medicine; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; fellow of the American College of Physicians; affiliated with Southern Baptist Hospital, Touro Infirmary, Charity Hospital of Louisiana, Hotel Dieu, and Mercy Hospital-Soniat Memorial; author of "Synopsis of Clinical Syphilis"; died April 2, aged 55, of coronary thrombosis.

Albrecht, Herman Fred ⊕ Detroit; Detroit College of Medicine and Surgery, 1916; died Feb. 4, aged 59.

Bartee, Luke Harvey, Port St. Joe, Fla.; University of Georgia Medical Department, Augusta, 1899; died Feb. 16, aged 81, of bronchopneumonia.

Bass, Harris Hartwell ⊕ Henderson, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1928; died recently, aged 50.

Carman, Richard Perry ⊕ Baltimore; University of Maryland School of Medicine, Baltimore, 1901; died Feb. 3, aged 85, of uremia.

Corpening, Flave Hart, Horse Shoe, N. C.; Jefferson Medical College of Philadelphia, 1928; died March 7, aged 50.

Cox, Harold Crisp ⊕ Hightstown, N. J. University of Pennsylvania School of Medicine, Philadelphia, 1926; past president of the Mercer County Medical Society; on the staffs of St. Francis Hospital in Trenton and the Princeton (N. J.) Hospital; died in the University of Pennsylvania Hospital in Philadelphia, Feb. 13, aged 52, of heart failure and hypertension.

Cruikshank, Omar Trees, Pittsburgh; University of Pennsylvania Department of Medicine, Philadelphia, 1901; died in VA Hospital, Aspinwall, recently, aged 78.

Eshleman, Lindley Heath ⊕ Marion, Ind.; Kentucky School of Medicine, Louisville, 1896; an Associate Fellow of the American Medical Association; at one time city health officer; past president of the Grant County Medical Society; past president of the Marion City Board of Health, of which he was secretary; affiliated with Marion General Hospital; died in Robert W. Long Hospital, Indianapolis, Feb. 28, aged 82, following an operation for gastric ulcer.

Hogan, George Archibald ⊕ Birmingham, Ala.; Birmingham Medical College, 1896; served on the faculty of his alma mater; died Feb. 21, aged 81, of pulmonary embolism.

Hooper, Vernon Jay, Los Angeles; Michigan College of Medicine and Surgery, Detroit, 1898; served during the Spanish-American War and World War I; for many years practiced in Detroit; died Feb. 7, aged 82, of bronchopneumonia.

Janney, Francis White ⊕ Baltimore; University of Maryland School of Medicine, Baltimore, 1905; an Associate Fellow of the American Medical Association; affiliated with Baltimore Eye, Ear and Throat Hospital; on the staff of the Cambridge (Md.) Hospital; died Feb. 1, aged 70, of heart failure.

Kahle, William D., Falls Mills, Va.; College of Physicians and Surgeons, Baltimore, 1911; died Feb. 4, aged 68, of coronary occlusion.

Klein, Rose Herchman, Hartford, Conn.; Woman's Medical College of Pennsylvania, Philadelphia, 1940; certified by the National Board of Medical Examiners; member of the American College of Allergists; affiliated with Mount Sinai Hospital; died recently, aged 50.

Lindsay, Samuel Sebastian, Manchester, Iowa; Bellevue Hospital Medical College, New York, 1891; died recently, aged 86, of cerebral thrombosis, chronic lymphatic leukemia, and arteriosclerosis.

Lurie, Sophie Arkadyevna ⊕ Los Angeles; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1913; member of the American Academy of Dermatology and Syphilology; died recently, aged 70, of carcinoma of the stomach.

⊕ Indicates Member of the American Medical Association.

McCubbin, Hardy Louis, Sacramento, Calif.; College of Physicians and Surgeons of San Francisco, 1899; at one time physician in charge of El Reposo Sanitarium in Reno, Nev.; died Feb. 26, aged 88, of cancer.

McCulloch, Horace Dwight, Toronto, Ohio; Ohio Medical University, Columbus, 1906; served as school physician and health officer; affiliated with Ohio Valley Hospital, Steubenville; died Jan. 20, aged 83, of thrombosis of the femoral artery.

McGarity, Joseph Arthur, Athens, Ga.; Medical College of Georgia, Augusta, 1916; died in Athens General Hospital Feb. 14, aged 65, of hypostatic pneumonia.

McLean, Daniel Calvin, Blytheville, Ark.; University of Nashville (Tenn.) Medical Department, 1910; on the staff of the Walls Hospital; died Feb. 10, aged 68, of thrombosis.

Meany, Thomas Edward ⊕ Chicago; Chicago College of Medicine and Surgery, 1909; fellow of the American College of Surgeons; formerly on the faculty of Loyola University School of Medicine; consulting orthopedic surgeon, Chicago State Hospital; died in St. Anne's Hospital March 21, aged 68, of cerebral hemorrhage and leukemia.

Miniggio, Antonio ⊕ Reno, Nevada; Regia Università di Torino Facoltà di Medicina e Chirurgia, Italy, 1900; a captain in the Italian Army during World War I; on the staffs of the Washoe Medical Center and St. Mary's Hospital, where he died March 27, aged 76, of pulmonary embolism following extensive contusion of the thigh and leg.

Mitchell, Carl Apperson ⊕ Benton Harbor, Mich.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1906; member of the Industrial Medical Association; an Associate Fellow of the American Medical Association; past president of the Berrien County Medical Society; served as city health officer and as a member of the board of education; served overseas during World War I; on the staff of Mercy Hospital; died in Tavares, Fla., March 17, aged 73, of coronary thrombosis.

Olmsted, Austin Orin ⊕ Green Bay, Wis.; the Hahnemann Medical College and Hospital, Chicago, 1902; past president of the Brown-Kewaunee Door Counties Medical Society; member of the Radiological Society of North America and the American Radium Society; for many years president of the board of education; died Jan. 14, aged 72, of carcinoma of the colon.

Park, William Edwin, Asheville, N. C.; Bellevue Hospital Medical College, New York, 1898; served during World War I; died March 9, aged 76, of cerebral thrombosis and arteriosclerosis.

Roberts, David Daniel ⊕ Enid, Okla.; Hospital College of Medicine, Louisville, Ky., 1906; past president and secretary of the Garfield County Medical Society; member of the American Association of Railway Surgeons; a medical officer during World War I; chief surgeon of Frisco, Rock Island, and Santa Fe railroads; served on the staffs of University Hospital and St. Mary's Hospital, where he died March 2, aged 75, of coronary occlusion.

Robison, Claude Alvin ⊕ Frankfort, Ind.; Indiana University School of Medicine, Indianapolis, 1918; on the staff of the Clinton County Hospital; formerly city councilman; died Feb. 2, aged 60, of cerebral thrombosis.

Rutledge, Harold Hunt ⊕ Richmond, Ky.; University of Louisville School of Medicine, 1936; served during World War II; member of the American Academy of General Practice; formerly connected with the health department of the state of Kentucky, director of Tate County Health Department, and health officer of Whitley and Madison counties; died in the General Hospital, Louisville, Feb. 11, aged 42, of a heart attack.

Schick, Martin F. ⊕ Fort Wayne, Ind.; University of the City of New York Medical Department, 1882; an Associate Fellow of the American Medical Association; on the staff of Lutheran Hospital; died March 10, aged 92, of heart failure.

Sinning, Charles Edward, Orlando, Fla.; Barnes Medical College, St. Louis, 1899; died Feb. 2, aged 77, of a heart attack.

Stith, Robert Boyd Jr. ⊕ Florence, S. C.; Duke University School of Medicine, Durham, N. C., 1935; certified by the National Board of Medical Examiners; chairman of the city board of health; served during World War II, and for exceptional and courageous conduct under fire on the Anzio Beachhead, Italy, was awarded the Bronze Star; on the staff of the McLeod Infirmary; died Feb. 13, aged 41, of coronary thrombosis.

Sumner, Gordon Sykes ⊕ Sylvester, Ga.; Atlanta School of Medicine, 1906; served in the Georgia State Legislature for 13 terms in the senate; died in Atlanta March 13, aged 69, of carcinoma of the prostate.

Taylor, William Ivey ⊕ Burgaw, N. C.; North Carolina Medical College, Davidson, 1902; died March 4, aged 76, of lobar pneumonia.

Teel, Ambrose Wilson ⊕ Redlands, Calif.; College of Physicians and Surgeons, Keokuk, Iowa, 1895; served during World War I; affiliated with Glendale (Calif.) Sanitarium and Hospital and the Los Angeles General Hospital; died March 24, aged 81, of an injury received in a fall.

Thompson, Clyde Coleman, Delhi, La.; Memphis (Tenn.) Hospital Medical College, 1911; died March 19, aged 70.

Tucker, Jesse E., Elizaville, Ind.; Physio-Medical College of Indiana, Indianapolis, 1895; died March 10, aged 83.

Wagenhals, Franklin Clark ⊕ Columbus, Ohio; Johns Hopkins University School of Medicine, Baltimore, 1913; emeritus professor of neurology at the Ohio State University College of Medicine; member of the American Psychiatric Association; died in Paris, France, March 16, aged 68.

Walker, Lewis Winston, Auburn, Miss.; Mississippi Medical College, Meridian, 1909; affiliated with McComb Infirmary, McComb, where he died March 30, aged 72, of acute enterocolitis.

White, Joshua Warren ⊕ Norfolk, Va.; Medical College of Virginia, Richmond, 1901; specialist certified by the American Board of Ophthalmology and American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; served during World War I; on the staff of St. Vincent's Hospital; died in Palm Beach, Fla., March 4, aged 77, of coronary thrombosis.

Widney, John Theodore Bland, Clovis, Calif.; Washington University School of Medicine, St. Louis, 1902; died in Fresno March 27, aged 74, of arteriosclerotic heart disease.

Wilbur, Herbert Lincoln ⊕ Joplin, Mo.; University Medical College of Kansas City, 1908; past president of the Jasper County Medical Society and the Newton County Medical Society; served during World War I; formerly city physician; affiliated with Freeman Methodist Hospital and St. John's Hospital, where he was past president of the staff, and where he died March 15, aged 76, of pulmonary and cerebral thrombosis.

Wilkinson, Michael Robert ⊕ Oconomowoc, Wis.; Northwestern University Medical School, Chicago, 1893; served as president of the Waukesha County Historical Society and as a director of the Oconomowoc High School; died March 15, aged 88, of chronic myocarditis and arteriosclerosis.

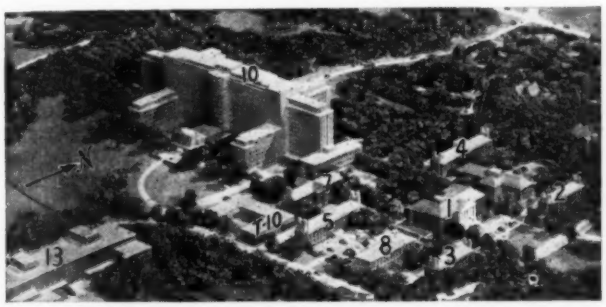
Wolff, Walter Hans ⊕ Massapequa, N. Y.; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1922; affiliated with Hospital for Joint Diseases; died in Meadowbrook Hospital, Hempstead, Feb. 7, aged 57, of congestive heart failure.

Yingling, Estey Cecil ⊕ Lima, Ohio; Starling Medical College, Columbus, 1906; formerly secretary of the Academy of Medicine of Lima and Allen County, of which he was vice-president and president; served during World War I; on the staff of Lima Memorial and St. Rita's hospitals; died Feb. 28, aged 72, of chronic lymphatic leukemia.

GOVERNMENT SERVICES

PUBLIC HEALTH SERVICE

Service Discontinued in Cleveland Hospital.—The U. S. Public Health Service Hospital, Cleveland, will discontinue admitting inpatients immediately, the Public Health Service announced May 20. An outpatient clinic will be established in downtown Cleveland as soon as the patients now receiving care can be discharged or transferred to other hospitals. The action was necessary because of the impending withdrawal of all patients of the Veterans Administration from the general and tuberculosis hospitals of the Service for the fiscal year beginning July 1. The 190 bed P. H. S. Hospital in Cleveland has been operating currently at a daily average census of 139, of which 55 are veterans. Removal of the veteran patients would reduce the daily average count to about 85, or 45% of capacity, and it would be impossible to operate the hospital efficiently and economically with such a low level of utilization. The Public Health Service will continue to provide medical care to merchant seamen, coast guardsmen, and other beneficiaries in the Cleveland area. The clinic replacing the hospital will be staffed by full-time personnel. Beneficiaries requiring hospitalization can receive treatment in the P. H. S. Hospital, Chicago. Public Health Service beneficiaries requiring emergency hospitalization in Cleveland will receive it in local hospitals at P. H. S. expense by contract arrangement.



The National Institutes of Health building no. 10 is the new Clinical Center.

New Clinical Research Center.—The newly completed Clinical Center of the National Institutes of Health is scheduled to admit research patients early in July. Located at Bethesda, Md., the center is a laboratory and clinical facility containing resources for the care and study of 500 patients. Occupancy will be gradual; it is planned to activate half the beds during the first year of operation and the remaining half during the second year. The Clinical Center will serve the seven National Institutes of Health, which form collectively the principal research arm of the U. S. Public Health Service. Thus, a clinical research dimension will be added to the Service's laboratory studies, which are concentrated for the most part on the major chronic diseases. For details see THE JOURNAL, Oct. 11, 1952, p. 541.

Personal.—Dr. Erval R. Coffey has replaced Dr. Richard F. Boyd as the medical director in the U. S. Department of Health, Education, and Welfare's regional office in Boston. Dr. Boyd is being transferred to San Francisco to fill the same position in the department's regional office. Dr. Coffey, an officer of the Public Health Service for 29 years, has been in Thailand for the past two years directing the efforts of 23 physicians, nurses, and sanitary engineers who made up the public health division of this country's technical mission to Thailand under the Mutual Security program.

NAVY

Conference on Submarine Medicine.—Experts on submarine medicine gathered for a conference May 13 at the Naval Gun Factory, Washington, D. C. The medical officers discussed problems associated with current apparatus now used by underwater demolition teams, diving equipment, and the physiological and psychological problems associated with this hazardous Navy work. In attendance were representatives of the Bureau of Medicine and Surgery; Naval Medical Research Institute, Bethesda, Md.; the Navy Medical Research Laboratory, Submarine Base, New London, Conn.; Underwater Demolition Group No. 2; the Force Submarine Medical Officer, Atlantic Fleet; and the Experimental Diving Unit, Naval Gun Factory. Plans were made for another meeting with civilian investigators in the field of submarine medicine. The proposed meeting will be held this fall.

Intern Training at Naval Hospitals.—The Surgeon General has announced that of the 176 Navy internships offered senior medical students who will graduate from medical schools throughout the United States in 1953, 169 have formally accepted assignments in Naval hospitals. Their training will begin July 1, 1953, and will be under the Navy's Graduate Medical Training Program. The students will be appointed lieutenants (junior grade) in the Naval Reserve Medical Corps, following graduation and will then be ordered into the active military service and assigned to Naval hospitals approved for intern training by the A. M. A. Council on Medical Education and Hospitals.

MISCELLANEOUS

Food and Drug Administration.—Retirement of John J. McManus, Atlanta district chief of the Food and Drug Administration, was announced May 31 by Charles W. Crawford, Commissioner of Food and Drugs, U. S. Department of Health, Education, and Welfare. Mr. McManus will be succeeded by Dr. Kenneth L. Milstead, now director of regulatory management in the FDA's Washington office. Dr. Milstead was formerly chief of the Cincinnati district. James C. Pearson, who has been assistant director of regulatory management since April, 1949, was named by Mr. Crawford as the new director. The division of regulatory management handles the preparation of scientific evidence for use in the trial of contested cases. In a tribute to Mr. McManus, Commissioner Crawford said, "Mr. McManus today closes a career of 45 years in behalf of pure, honestly labeled foods, drugs, and cosmetics. It has been one of genuine and fruitful service to the American people."

New Headquarters for National Science Foundation.—The National Science Foundation has moved to a new location, 1520 H. Street, N.W., Washington 25, D. C. The new headquarters are in the old "Cosmos Club" building, recently taken over and renovated by the General Services Administration. The new telephone number is STerling 3-2140. The government telephone code is 1224. The government messenger service code remains Stop 19. There is no change in the Western Union desk-fax call letters QBM. The mailing address will continue to be National Science Foundation, Washington 25, D. C.

VETERANS ADMINISTRATION

Personal.—Dr. Lee H. Schlesinger of Clarksburg, W. Va., has been appointed manager of the new VA Hospital in Chicago (West Side), and Dr. Walter S. Pugh of Providence, R. I., has been named manager of the VA Hospital in Erie, Pa. The West Side hospital in Chicago, a 496 bed general medical and surgical installation, is scheduled to open late this summer.

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FOREIGN LETTERS

AUSTRALIA

Administration of BCG Vaccine.—BCG vaccine has to be obtained from the Commonwealth Serum Laboratories at Melbourne, to which it is necessary to give two weeks' notice. The order has to be placed through the health department in the state concerned. The vaccine is delivered by air, and must be collected immediately from the airplane, placed in a refrigerator, and used within the next 24 to 36 hours. Before a person can receive BCG vaccine it is necessary for him to be Mantoux-tested on two occasions at six week intervals. Roentgenography of the chest is an essential preliminary. Four weeks after the BCG vaccine has been given, the reaction is read and noted. Four weeks later another Mantoux test is done, and further Mantoux tests are required at six month intervals. The Commonwealth Serum Laboratories refuse to supply BCG vaccine unless this technique is adhered to. Complete records have to be kept on a special card.

Kodak Finances Medical Research.—Between one-quarter and one-third of the profit of Kodak (Australia) Pty. Ltd. is now devoted to medical research in Australia. This is due to the philanthropic activities of the joint founder of the Australian organization, Mr. Thomas Baker, who died in 1928. A perpetual trust fund was established in that year known as the Thomas Baker (Kodak), Alice Baker, Eleanor Shaw Benefactions Fund. The medical research institute at the Alfred Hospital, Melbourne, bears the name of the benefactors, but is usually known as the Baker Institute of Medical Research. The institute has made valuable contributions to medical knowledge in a wide variety of medical fields. Possibly the most outstanding scientist who has worked in the laboratories of the institute has been Willis, the pathologist, now at Leeds.

Medical Education.—Americans have an enthusiasm for education that is lacking in Australians, stated Prof. W. B. MacFarlane, who is professor of physiology in the University of Queensland. He recently returned from a visit to the United States. He reports that 1.3% of Americans are students at colleges and universities, a much higher proportion than in Australia. At present 1 American in 80 is at a college or a university. In Queensland the number is about 1 in 350. Americans spend $10 per person per year on higher education compared with about $1.10 in Queensland. In the United States students spend between $500 and $1,000 per year to attend medical schools. In Queensland they pay about $110.

Rare Chloramphenicol Complications.—There has been no evidence in Australia of serious complications following the use of chloramphenicol. On the other hand, this drug has been the mainstay of treatment of gastroenteritis in children, especially in Queensland, where infections by a Salmonella microorganism caused a high death rate in an epidemic in 1946-1947. The second epidemic, three years ago, was controlled by the use of chloramphenicol. A watch has always been kept on the blood cell count of children being treated with this drug, and if a tendency for the count to fall is detected the therapy is stopped.

Record Incidence of Diabetes.—Sydney has one of the highest diabetes rates in the world, stated Dr. R. D. Lawrence, world authority on diabetes, and physician to the Kings College Hospital in London. Two per cent of Sydney's population have diabetes, compared with one-half per cent in England and one and one-half per cent in the United States. Dr. Lawrence ascribed this high incidence to overeating.

The items in these letters are contributed by regular correspondents in the various foreign countries.

DENMARK

Hospital Costs Then and Now.—The Aalborg County Hospital has been studied by E. Schiödt for a comparison of the financial years 1913-1914 and 1951-1952. There was a sevenfold increase in the number of patients, a rise from 906 admissions in the first period to 6,518 in the second. Much greater use was made of the hospital beds in the second than in the first period, each bed standing unoccupied only 10 days in the second period, while the corresponding figure for the first period was 85. The total sum spent in the second period was 22 times greater than that spent in the first period, but the expenditure per patient was only 3 times greater; when the purchasing value of the krone in the two periods was taken into account, hospital treatment in reality had become cheaper. To understand this conclusion it should be made clear that the average duration of residence in hospital was reduced from 42 days in the first period to 18 in the second. In the period under review the number of physicians employed by this hospital had risen from 3 to 21, and that of nurses and student nurses from 34 to 136. Yet the number of patients per physician remained practically unchanged, with 302 in the first period and 310 in the second. On the other hand, there was a considerable rise in the number of patients treated per nurse, from 27 to 48. In the first period salaries for the staff accounted for only 17% of the total cost, whereas they did so for 44% of the total cost in the second period.

Between the two periods studied there was a profound change in the indications for admission to hospital. With the discovery of penicillin scarlatina patients need no longer be admitted to hospital. For much the same reason patients with pneumonia have now become rare in hospital. On the other hand, a new group of patients is now being admitted to hospital for treatment with antibiotics and corticotropin (ACTH). The circulation of patients in hospital is now speeded up, with both surgical and medical patients being discharged with a view to their treatment being completed at home by general practitioners. This means greater cooperation between the physicians in hospital and outside it. Schiödt, whose study is published in *Ugeskrift for laeger* for March 5, 1953, concludes that the experiences of Aalborg County Hospital may be regarded as typical of other Danish public hospitals.

Medical Students in Place of Iron Lungs.—Brief reference has already been made in THE JOURNAL (**151:**1126 [March 28] 1953) to the part played by medical students when Copenhagen was overtaken by a catastrophic outbreak of poliomyelitis in the autumn of 1952. The 500 beds of the Blegdam Fever Hospital soon proved inadequate and had to be supplemented by numerous beds in other hospitals. Early in the outbreak the Danish and foreign narcosis specialists were unable to cope with the calls made on them for artificial respiration. Towards the end of August the first appeal for volunteers was made to the Medical Students' Council, which was asked to supply 10 students to help with the bag ventilation of patients. Their task was considered so responsible that at first only senior medical students were asked to volunteer. Some 150 did so in September, and they were organized in teams of 4 or 5 students each. By the end of September the supply of senior students proved insufficient, and junior students were called on, with some misgivings. They rose to the occasion, doing excellent service after mastering the necessary technique and precautions to be taken. Early in November the supply of medical students had been exhausted, and Professor Lassen, who is in charge of the Blegdam Hospital, sent out an appeal to the dental students. More than 200 of them answered this appeal, with the result that the time each student had to spend in hospital could be reduced.

Altogether some 1,400 of the some 1,700 medical students in Copenhagen took part in this work and were paid at the rate of about 30 shillings for eight hours. This modest remuneration may seem trifling in comparison with the clinical

experience and insight into the nursing of the sick gained by these students as they worked hour after hour with a patient. In recognition of the services of these students and other members of the staff of the Blegdam Hospital, the municipal authorities of Copenhagen, headed by the Burgomaster Julius Hansen, addressed a letter of thanks to the Danish Medical Association. Some figures published by the burgomaster are a concrete expression of the calls made on the hospital. Though its budget allows for 27 physicians, it actually employs 60, of whom 15 are narcosis specialists. The budget provides for some 265 nurses, whereas the actual number of nurses employed is 625. In October payments made to students amounted to about 150,000 kroner. On Nov. 5 some 600 patients with paralytic cases of poliomyelitis were under treatment. These figures tell little of the epic of the medical students of Copenhagen in the autumn of 1952.

SPAIN

International Congress of Therapeutics.—More than 1,000 members attended the Third International Congress of Therapeutics held recently in Madrid. Among the official topics were potassium and the use of radioactive isotopes.

Potassium.—Prof. Z. M. Bacq of Belgium stated that according to Hodgkin's technique the intracellular concentration of potassium in excitable tissues is a passive phenomenon, secondary to the active secretion of sodium ions. It can be proved that the erythrocytes of human blood actively eliminate sodium and passively concentrate potassium. It is known only that they do not function when glycolysis is not normal.

Drs. R. Hazard and J. Hazard of France, in a résumé of their work, stated that the normal potassium of the body has complicated actions, the direction of which may change in accordance with the concentration in which potassium is used up by the body, and also in accordance with the antagonism or synergism that the substance encounters in the body. Potassium intervenes in the metabolism of glycides, similar to the manner of glucose when the latter is present as a reserve. Potassium takes a part, also, in the metabolism of protids and in regulating the acid-base equilibrium. Hypopotassemia causes alkalosis, the control of which depends mainly on the proper secretion of active substances of the suprarenal cortex. Secondarily, it is controlled by the suprarenal medullary hormone and by the mechanism of renal elimination. From a pharmacological point of view, potassium can be either useful or dangerous, depending on the concentration in which it acts. Its toxicity varies with the degree of initial concentration of its salts. Potassium is dangerous to the heart when its level of concentration in the blood is so high that it cannot be rapidly lowered by elimination through the kidneys. Potassium, even in small doses, has a stimulating effect on the central nervous system when it contacts the cerebral cells. In higher concentration it produces inhibition of the medullar and bulbar centers. It is closely related to epinephrine and acetylcholine, the chemical intermediary substances that stimulate the autonomic nervous system. Potassium is indispensable to the production of parasympathetic stimulation. The vagal stimulation results in the liberation of both potassium and acetylcholine, whereas the sympathetic stimulation results in liberation of potassium, epinephrine, and some other sympathins. The potassium ion has a biphasic effect on the muscular system. It stimulates liberation of small doses of potassium and prevents liberation of large doses by a mechanism of double circuit between acetylcholine and potassium, each of which stimulates liberation of the other at the level of the muscle. Potassium is indispensable for the contractility of the heart; however, the toxic effect appears when the concentration of potassium is above the useful level. The changes of the electrocardiogram, as caused by either hypopotassemia or hyperpotassemia, are well known. The potassium ion, when in low concentration, favors excitability of the motor nerve fibers by preventing the activity of high concentrations. The inhibitory action easily appears on the sensory nerve fibers, and certain potassium salts increase the activity of local anesthetics. On the smooth fibers of the intestine the potassium ion seems to cause liberation of acetylcholine, potentiation of the tonic effects of this substance, and stimulation of muscular action. In relation to antagonistic substances, the speakers pointed out that the calcium ion is the most active and the commonest antagonistic substance. It acts on the central nervous system, on the autonomic nervous system, on neuromuscular excitability, and on the heart. The antagonism may even result in changing the effects of digitalis, and as calcium increases potassium decreases.

Drs. G. Bickel and H. C. Plattner of Switzerland reported the results of studies made on all the syndromes of hyperpotassemia and hypopotassemia. The pathogenetic factors, clinical forms, changes seen on the electrocardiogram, and the diseases most commonly complicated by these syndromes were discussed. There is a form of hyperpotassemia of renal insufficiency with oliguria or anuria and other forms in hemolytic and traumatic syndromes, in diabetic coma, and in Addison's disease. There are also different forms of hypopotassemia in diarrheal syndromes, in hypoglycemic coma, in nephritis, in the Cushing's syndrome, and in syndromes caused by administration of large doses of corticotropin, desoxycorticosterone, and cortisone. The forms of hypopotassemia caused by administration of large doses of sodium salts and those that are a complication of pyloric stenosis, of obstruction of the upper segments of the intestine, or that follow an operation, were also discussed.

Prof. F. Rietti of Italy stated that the basal potassium is of clinical value in the majority of cases, although it does not always reflect the actual condition of the intracellular potassium. The syndromes associated with hyperpotassemia are always graver than those associated with hypopotassemia. The changes in the electrocardiogram have a definite clinical value, but the electrocardiogram cannot replace the laboratory determinations of potassium in the blood. The main factors of hypopotassemia are fasting, an insufficient supply of potassium to the body, rapid elimination of the substance through the kidneys, post-therapeutic diabetic acidosis, hyperactivity of the suprarenal cortex, vomiting, diarrhea, dilution of the extracellular fluids as a result of administration of solutions that do not contain potassium, and the use of certain drugs. The speaker described some cases of cryptogenetic chronic hypopotassemia, which is very rare. The pathological changes of potassemia are always due to acute diseases.

Drs. E. Jaso and E. Iturriaga of Madrid reported results of their investigations conducted on the significance of potassium in pediatric diseases. The symptoms of hypopotassemia in children consist of muscular hypotonia, deep hyporeflexia that in some cases progresses into actual paralysis, meteorism, and paralytic ileus. There are changes in the electrocardiogram, and the figures of potassium in the blood plasma are low. Diarrhea in infants, hypertrophic stenosis of the pylorus, congenital alkalosis with diarrhea, infantile steatorrhea, and bulbar poliomyelitis are specific pediatric diseases that develop with a deficiency of potassium. Potassium therapy is indicated in any of these diseases. The deficiency of potassium in infantile diarrhea is due to (1) a loss of potassium through the feces, vomiting, and perspiration; (2) a diminished amount of potassium administered in the diet, or a lack of administration of the substance; (3) administration of salt solutions in therapy of dehydration; and (4) the changes of the intracellular exchange caused by sodium. In the early period of these diseases the amount of potassium in the blood serum is large in about 25% of the cases. The increase is due to liberation of potassium by the tissues. Later, hypopotassemia follows and the amount of potassium in the muscular tissues is small, as found by determinations carried on by the speakers. Some of the children observed by the speakers had potassium therapy in association with the treatment of the given disease. The rest of the children were the controls. The clinical course of the disease was about the same in both groups of children. The electrolyte shock was controlled sooner in patients who had potassium therapy than in the controls. There were early hypoproteinemia and hypoalbuminemia. Total hypoproteinemia developed in children with acute dystrophy. The figures of the gamma globulin fraction increased. The increase was so sharp in certain cases that the figures were four times higher than normal. In patients in either group, namely, those who had potassium therapy and those who did not, the figures of

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chloremia were low during shock and normal after it. The hematocrit value and the number of erythrocytes followed the standard of the disease in the given case, without changing with the administration of potassium. From a statistical point of view, the speakers were unable to confirm previous reports in the literature on the good results of potassium therapy in toxic diarrhea of infants. The figures obtained by the speakers in children who had potassium therapy can be superimposed on those observed in the controls (a 13% rate of mortality). In the administration of potassium the speakers followed Darrow's scheme of dosage. They administer the substance either by parenteral or oral route. In certain cases they used the mixture advised by Gosta-Davidsen. In toxicosis of infants, the speakers warned against the administration of potassium serum on the first day of the disease because of the fact that hyperpotassemia is present on that day. Only when one can prove that there is hypopotassemia should potassium serum be given. When the patients show toxic symptoms after therapeutic administration of potassium, the speakers advise to resort to a combined treatment of dextrose, insulin, and calcium.

Drs. Di Guglielmo and Vallecorsi reported results of studies on the contents and distribution of potassium in the body and the techniques of administration of potassium salts. They advised the use of potassium chloride, which contains about 50% potassium, can be sterilized without difficulty, and can be administered by any route. Also, gluconate, citrate, and phosphate can be used. The speakers resorted to the administration of potassium in certain diseases without hypopotassemia, namely, in certain cardiac diseases (hyposystole, ventricular tachycardia, and extrasystolic arrhythmia), in arterial hypertension (with moderate and uncertain effects), and in certain diseases of the muscles, without hypopotassemia. It can also be given as a diuretic, but the administration of the substance is dangerous in cases of oliguria of renal origin; it is frequently given in cases of bronchopulmonary allergy, pleurisy, adenitis, and arthritism, and as a solvent of antibiotics.

Dr. Castro Mendoza reviewed the various techniques used in the determination of potassium. The most exact and sensitive microdetermination is that of precipitation with chloroplatinic acid, which is comparable to the macrogravimetric methods. For clinical uses, the procedures using cobaltinitrite are sufficient, although the limitations of exactness of these procedures are well known. For the final titration, ceriometry or colorimetry of the cobalt ion can be recommended. Spectrometry is not sufficiently precise for common use, although it has a great sensitivity. In photometric evaluations, the flame photometer has the advantage of the rapidity with which the evaluations can be made. This method permits one to work in large series, although its exactness is not as accurate as that of the method of the chloroplatinic acid. Some other methods, such as the precipitation with phospho-12-tungstate, dipicrylamine, and others, are still very new and not widely used.

Massive Hormonal Therapy.—Dr. Perez Vitoria of Barcelona suggested changing the term retarded hormonotherapy to slow hormonotherapy. This therapy is indicated when it is advisable to prolong the effect of the hormones. It is also indicated in cases of acute endocrine disturbance and in cases in which it is necessary to reduce the number of injections to make an economical treatment. The retarded forms of hormonal therapy include only insulin, epinephrine, posterior pituitary injection (Pituitrin), testosterone, estrogens, progesterone, androstranediol, desoxycorticosterone, cortisone, and corticotropin (ACTH). Frequently its results are much better than those of other ordinary forms of therapy. The preferable form of the substance to be used is microcrystals. The tablets of the substance are to be rejected for implantation.

Dr. N. Pende of Italy reported the results of his studies on the various methods of hormonal therapy. Pende states that the implantation of tablets of crystallized hormone (as restricted to desoxycorticosterone, testosterone, estrone, and progesterone) gives transient results, making it necessary to repeat it several times. Frequently the testosterone tablets are eliminated through the operative wound because of colliquation of the tissues. Tablets of estrogens produce metrorrhagia, and the danger of hyperdosification cannot be avoided. The best results of implantation are obtained in cases of Addison's disease, and the most inconstant results are observed in hypogonadism in men. The speaker stated that the depositing of hormone crystalline suspension offers no advantages over parenteral injections because the velocity and quota of absorption are unknown and in cases of hyperdosage it is not possible to remove a portion of the introduced hormones. The technique of administration of hormonal therapy either by ingestion (preparations of thyroids or of estrogens) or by parenteral route (total extracts or single hormones) is difficult. Frequently the practitioner gives to the patients excessive doses (androgens and estrogens). It is convenient to give small doses to the patients and, especially, to apply topic treatment near the tissues on which the hormones should act (urethra, vagina, breasts, and nasal structures).

Prof. G. Marañón of Spain reported the results of his studies on three problems: (1) the reason for the administration of moderate doses of hormonal therapy, (2) the inconveniences and dangers of the administration of large doses, and (3) the most adequate technique of administration of hormonal therapy. 1. The goal of hormonal therapy is to obtain the maximum results of physiological effects. For these results to be obtained two conditions are necessary, namely, that the dose of hormones administered be of about the same quantity as that of the normal secretion of the glands, and that the time at which the therapy is given be about the same as that at which the given glands are liberating their secretions. The therapy should be given in accordance with the needs of the body and not with an arbitrary schedule. Moderate doses are the most normal. Nearly all the favorable effects that are obtainable from hormonal therapy can be obtained with moderate doses and without therapeutic haste. It is difficult for the physician to discover the exact moment at which the effect of the hormones should be felt, except in certain cases, as in that of insulin in which the time of action is well known. 2. Entirely antiphysiological large doses of hormones may result in the production of unpleasant and harmful effects. In certain instances they may cause hyperfunctional reactions in the corresponding gland; in some other cases they may cause functional changes and even lesions of other endocrine glands; still in other cases they may produce nonspecific and nonglandular pathological disorders, which seem to be due to rupture of the balance of adaptation that the given glandular insufficiency had already created. 3. The most adequate technique for administration of hormonal therapy is the implantation of tablets or the injection of microcrystals, which at the present time should be restricted to a small number of hormones. The reason for the administration of hormones by this technique is that the therapy is of substitution and the effects are similar to the physiological action of the hormones.

Prof. L. de Gennes of Paris discussed hormonal therapy of cancer of the breast. The treatment is palliative and coadjutant when it is resorted to early in the course of the disease, but it does not replace direct surgical treatment or roentgen therapy of the tumor. The speaker stated that hormonal therapy should be administered as complementary treatment, as well as for the prevention of metastasis or else as a palliative measure when metastases have already appeared, in order to slow their growth, diminish pain, and prolong the life of the patient. The effects of ovariectomy on cancer of the breast are better than those of roentgen therapy on the ovary. Ovariectomy diminishes the percentage of recurrences, acts on the bone metastases (especially on the vertebral metastases), and improves the general condition of the patient. The androgens, when administered in large doses, moderately act on the tumor and on the metastases of the soft tissues, but they have energetic effects on the bone metastases and on the pain that these metastases produce. The doses should be large because of the fact that the small doses are almost inactive and are harmful. The estrogens are more active on the tumor of the breast, which may even diminish in size. They are also active on ulcerations, adenopathies, and metastases; however, they should be reserved for administration only to old women or to women in well-established menopause. Even in women in these groups the bone metastases are more favorably effected by androgens than by estrogens. Young women with inoperable cancer of the breast should have castration and androgens in massive doses. In men castration and estrogens sometimes give similar results to those obtained in cancer of the prostate, although they are not as constant and dramatic as those observed in

the latter form of cancer. It is difficult to state whether or not the therapy with these hormones has actual prophylactic value and also if the therapy diminishes the number of recurrences when it is given after early operation in cases of cancer of the breast without axillary involvement; however, it seems that preventive androgenic therapy of mastitis prevents cancer transformation in a certain number of cases. Surgical castration improves the prognosis of cancer after late operation, but similar results are obtained from the administration of injections with massive doses of testosterone. The association of both surgical and hormonal therapy gives promising results, although they are not constant and vary with the given case. It is difficult to evaluate the actual effects of hormonal therapy in cancer, which is a disease that is very uncertain and prone to complications of an unpredictable course, the apparent improvement of which is often followed by spontaneous regression of the disease. Hormonal therapy in cancer of the breast is a real improvement; however, the biological mechanism of the improvement of the disease under the effect of the hormones is still unknown. The study of this mechanism will result in the discovery of the origin and course of hormonal cancer.

Radioactive Isotopes.—Prof. C. Gil y Gil of Spain reviewed the general subject with a rather pessimistic point of view because of the dangers of improper handling of these substances. The speaker made special reference to the work of American researchers. Radioactive isotopes have not been used very much in Spain.

Prof. A. S. McFarlane of England reported the results of his studies on radioactive isotopes on metabolic conditions, as shown by the results obtained by American researchers. The point of view that the liver is the main organ producing plasmatic proteins is confirmed by the fact that, following the introduction of amino acids marked with radioactive carbon in the arterial blood of the liver of isolated and perfused rats, a normal production of albumin and globulin takes place in the blood. It is observed, by studying the radioactivity of free amino acids and proteins of the plasma of rabbits, that the liver acts rapidly on free amino acids, transforming the greater part of them to plasmatic proteins within two hours; however, if amino acids are introduced in larger quantity to that corresponding to the physiological velocity in the production of proteins, the amino acids in excess are directly oxidized in the tissues. The plasmatic proteins, which are synthetized in the liver in 2 hours, require 12 more hours to diffuse themselves outside of the liver and to reach a uniform concentration in the plasma and in the lymph. Later on, they pass unchanged from the lymph to the cells of the tissues and become slowly oxidized at about the same time they are consumed in the oxidization of the intracellular proteins in the tissues. If an excessive amount of amino acids is given to the tissues, they become stored in the tissues. This period lasts for several weeks, during which time the tissues begin to hydrolyze the excessive amino acids. The proteins of the liquid of ascitis are identical to those of the plasma, and they are in constant equilibrium with the latter through the peritoneal membrane.

Dr. E. E. Pochin of England stated that frequently it is very important to evaluate the distribution of the isotopes in the different parts of the body and to detect them in the organs in which they are stored. He describes the following methods for evaluating the distribution of the isotopes: (1) using a meter for counting the irradiations, which is provided with a lead cylinder for protection and which is very useful in the regulation of the therapy with radioactive gold, (2) using the method used for the treating of hyperthyroidism with radioactive iodine, with a special protected meter, and (3) measuring the outline, which combines some of the advantages of the previously mentioned methods and is of great value in detecting the areas of abnormal concentration of iodine in carcinoma of the thyroids and also for obtaining quantitative tests for the progress of course of the disease.

Dr. M. Tubiana of France discussed the treatment of thyroid diseases by means of radioactive iodine. He reported the results observed in the treatment of 80 patients with hyperthyroidism and 35 patients with cancer of the thyroid. The treatment with radioactive iodine gave excellent results in 75% of the patients with hyperthyroidism. In 55% of the cases the results were obvious after administration of the first dose. The results were incomplete in 11% of the cases and poor in 12% of the cases. In comparing the clinical results with the doses of radiations given to the patient, the speaker observed that the best results are obtained with a dose varying between 7,000 and 10,000 r, that is a dose of about 0.1 mc. of radioactive iodine for every gram of thyroid, as fixed in 24 hours. When rapid results are desired the dose should be greater. This is the case of patients with cardiac diseases in whom the establishment of a lasting hypothyroidism is feared. The speaker did not observe serious accidents, but late accidents may occur. The treatment with radioactive iodine is indicated in all cases of failure and contraindication of surgical treatment, especially in patients with cardiac diseases or with deficiencies, as well as those who cannot stand prolonged chemotherapy and those who refuse to have an operation. The inconveniences and dangers are less, in the majority of the cases, than those of a surgical intervention; however, the speaker advised this treatment only in patients over 35, as there is the possibility of the occurrence of late dangers, which up to now are unknown. The treatment with radioactive iodine is indicated in cases of cancer of the thyroid when the cancerous tissues fix sufficient amounts of iodine. It is necessary to make determinations of iodine and biopsies. Out of a total number of 140 patients with cancer of the thyroid observed by the author the treatment was given to 35 patients, with excellent results in 8 cases. The results of this statistical study show that the number of patients who obtain benefit with this treatment is relatively small.

Dr. J. T. Van der Verff of Holland reported results of the treatment in patients with polycythemia, leukemia, and other disorders of the reticuloendothelial system. The results obtained in the patients observed by the speaker were in disagreement and never curative. A great improvement is observed in patients with polycythemia vera, and the patients enjoy an almost normal life. Radioactive phosphorus, when given with careful observation of the patient and in combination with some other procedures, is of value, although it does not prolong the duration of the span of life of the patient. In some other disorders of the reticuloendothelial system the response of the patients to the treatment varies in different cases. The dangers of radioactive isotopes make it advisable to reserve this treatment only for patients who do not react well to other means.

Dr. P. H. Hahn of the United States discussed the problem of the treatment with radioactive isotopes in tumors and tumoral processes. He considered the use of gold therapy in four different categories: (1) intravenous administration by means of which the reticuloendothelial system is provided with selective irradiation in diffuse diseases of the macrophagic lymphoid system, (2) interstitial use of the colloid, (3) introduction of gold colloids in several cavities of the body, and (4) introduction of gold colloids, sometimes modified, in the tissues or regions of the body. The intravenous administration of manganese and gold colloids is especially efficacious in chronic leukemia. In some cases of Hodgkin's disease the treatment can give palliative results, although they are not definitive. The treatment with interstitial colloidal gold will be very much in use in the near future. It will be resorted to in certain common forms of malignant tumors, such as cervical, mammary, prostatic, testicular, and cranial tumors as well as in other tumors deeply located, as coadjutant therapy of surgery. At the present time, the intracavitary use of gold colloids is the most popular. The treatment is palliative after surgery. It has been demonstrated that free tumoral cells are susceptible, in experimental conditions, of treatment by means of these procedures. The introduction of protected gold or of protected gold colloids in regions from which tumoral particles are to be eliminated by means of the lymphatic drainage constitutes a potential method of controlling certain types of malignant metastases, especially in cases of carcinoma of the uterus and of bronchial cancer.

The success of this congress constitutes an international homage to Dr. Teófilo Hernando, professor of therapeutics in the Faculty of Medicine of Madrid for more than 30 years. Dr. Hernando is the president of the Society of Gastroenterologists of Spain. After the Civil War in Spain, he was politically deprived of his professional activities. He was restituted to his chair by the academic authorities shortly before he reached the age of retirement, according to the law.

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CORRESPONDENCE

DIAGNOSTIC USE OF PENTYLENETETRAZOL (METRAZOL) IN ACUTE BARBITURATE POISONING

To the Editor:—There is unanimity of opinion that many cases, probably the majority, of acute barbiturate intoxication require only good symptomatic therapy (Koppanyi, T., and Fazekas, J. F.: *Am. J. M. Sc.* **224**:577, 1952). Numerous pharmacologists and clinicians, however, have demonstrated that, in severe barbiturate poisoning in animals (Tatum, A. L.: *Physiol. Rev.* **19**:472, 1939) as well as in humans (Koppanyi, T., and Fazekas, J. F.: *Am. J. M. Sc.* **220**:559, 1950), certain central analeptics are of lifesaving value. The problem is the selection from the numerous cases of acute barbiturate poisoning of those requiring specific analeptic therapy. The history, barbiturate blood levels, and physical signs cannot always be relied on; in fact, in many instances, the history and blood levels may not be available to the physician and are, sometimes, misleading. Schmidt, in 1945, and Fazekas and Bessman, currently, have noted, in both animals and human beings, a lowered cerebral metabolic rate associated with deep barbiturate coma but not necessarily with light barbiturate anesthesia.

We have introduced the concept that an orientation dose of pentylenetetrazol (Metrazol), when given intravenously to patients with acute barbiturate intoxication, may awaken or cause a return of reflexes in those patients only lightly or moderately depressed. These patients very often show a permanent improvement after a single orientation dose (5 cc. of a 10% solution). If no improvement follows such an orientation dose, the patient should be given more intensive therapy.

Cerebral Blood Flow and Metabolic Rates Before and After Administration of Pentylenetetrazol

	Cerebral Blood Flow, Cc./Min./ 100 Gm. of Brain	Cerebral Oxygen Consumption, Cc./Min./ 100 Gm. of Brain	Cerebral Arteriovenous Oxygen Difference, Vol. %
Average normal values *.....	54.2	3.5	6.47
Before pentylenetetrazol.....	30.3	0.9	2.92
After pentylenetetrazol (17 hr.).	58.8	3.0	5.12

* Previously established for normal subjects.

We have employed the orientation dose of pentylenetetrazol for many years, and it has proved to be an invaluable guide in outlining subsequent therapy. For example, a 48-year-old man had taken an undetermined amount of a barbiturate intending suicide. He was first seen three hours after ingestion of the drug. He was treated symptomatically; pharyngeal airway oxygen, fluids, and penicillin were administered for 24 hours. After the first 24 hours, the house staff became concerned about his condition because he was still without reflexes, he was comatose, and he did not respond to noxious stimuli. Studies of cerebral blood flow and metabolism were undertaken and showed a marked depression of both values. The patient was then given a 10% solution of pentylenetetrazol intravenously at a slow rate. After the injection of 3 cc., the patient's reflexes returned within five minutes; he lifted his head spontaneously and attempted to speak. From the responses obtained, it became obvious that this patient required only symptomatic therapy. Despite the small amount of pentylenetetrazol given, he did not relapse into his former comatose state but continued to improve. In three hours he was fully conscious. Seventeen hours later the cerebral blood flow and metabolism were again determined and were found to be normal (see table).

This case is particularly interesting because not only the physical findings but also the cerebral blood flow and metabolism were indicative of deep (barbiturate) depression, although the response to pentylenetetrazol indicated only a light depression. It is, therefore, suggested that the response of a patient to an orientation dose may be an even more reliable index than the cerebral metabolic rate. If an orientation dose of pentylenetetrazol were universally administered in acute barbiturate poisoning, more reliable statistical information could be gained as to the efficacy of central nervous system stimulants in the treatment of human barbiturate intoxication.

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OPTIC NEURITIS

To the Editor:—With respect to the clinical note in The Journal, April 18 (page 1403), it is not unusual, in patients with cardiovascular disease, to find both anemia and optic neuritis associated with subacute bacterial endocarditis. For example, Friedberg states: "Optic neuritis and even choked disk have been described as toxic manifestations of the disease" (that is: bacterial endocarditis) (*Diseases of the Heart*, Philadelphia, W. B. Saunders Company, 1949, p. 791). Kauntze has published a report of seven cases of subacute bacterial endocarditis in which optic neuritis occurred (*Brit. Heart J.* **9**:34, 1947). Statements in "Genetics in Ophthalmology" by Sorsby and "Clinical Neuro-Ophthalmology" by Walsh confirm this fact, described first in the classic paper by Falconer entitled "The Importance of Optic Neuritis and Retinal Hemorrhages in the Diagnosis of Chronic Septic Endocarditis" (*Quart. J. Med.* **3**:107, 1910).

The omission of reference to these facts from the clinical note should be called to the attention of clinicians who encounter this condition, since, under the circumstances, it is not possible to ascribe optic neuritis to chloramphenicol or to any other drug; on the contrary, it must be considered one of the possibilities to be looked for and treated as part of the disease entity.

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PROTEIN SYNTHESIS AND CORTISONE

To the Editor:—In the April 18, 1953, issue of The Journal, an editorial on protein synthesis and cortisone concludes that the effect of cortisone "is that of over-all suppression of tissue protein synthesis." It is true that, in effect, this is the net result of the administration of this drug to animals. We feel, however, that there is enough evidence to lend support to the statement "Adrenal cortical secretions accelerate protein catabolism by a direct action on the oxidative enzymes for deaminating amino acids." This action has been demonstrated in vitro with supportive in vivo data (*J. Biol. Chem.* **183**:11, 1950) and has been repeatedly confirmed (*Ann. Rev. Physiol.* **15**:402, 1953). More recent clinical observations in patients with Addison's disease (*J. Clin. Endocrinol.* **13**:429, 1953) have supported this thesis by demonstrating a decreased capacity of these patients to metabolize amino acids administered intravenously.

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Postgraduate Continuation Courses for Physicians

Compiled by the Council on Medical Education and Hospitals for the Period July 1, 1953, to Jan. 15, 1954

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Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	ALLERGY		
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Personal Course in Allergy	Arranged, 6 months, full time	$500.00
	Personal Course in Allergy	Arranged, 1 month, full time	200.00
	Personal Course in Allergy and Related Conditions	September 23, 10 days, part time	125.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Montefiore Hospital	Medicine PM 68 Allergy	September 17-December 10, once weekly, part time	50.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Allergy	Arranged, 2 months, part time	50.00
New York Polyclinic Medical School and Hospital, 345 West 50th St., New York 19, New York	Allergy	Arranged, twice weekly, part time	50.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	Allergy 5415-A	November 9-13, full time	100.00
Albert Einstein Medical Center, Southern Division, 5th and Reed Sts., Philadelphia 47, Pa.	Allergy	Fall, once weekly, part time	75.00
	ANATOMY		
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Surgical Anatomy	September 28-June 2, twice weekly, part time	250.00
	Surgical Anatomy	September 30-June 2, once weekly, part time	100.00
University of California Medical Extension, 10851 LeConte Ave., Los Angeles 24, Calif.	Surgical Anatomy	September-December, once weekly, part time	75.00
Mercy Hospital, San Diego 3, Calif.	Anatomy	Twice weekly, 30 weeks, part time	None
San Diego County General Hospital and Mercy Hospital, San Diego 3, Calif.	Anatomy	October-August, part time	[44]
University of Maryland School of Medicine, 29 S. Greene St., Baltimore, Md.	General Anatomy [45]	Arranged during academic year, full time	Arranged according to content and duration of course
	Surgical Anatomy	January-June, twice weekly, 15 weeks	150.00
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1]	Neuroanatomy	October, 12 weeks, twice weekly, part time	100.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Applied Anatomy for the General Surgeon	Arranged, 250 hours, part time	375.00
	Anatomy of the Thorax	Arranged, 100 hours, part time	150.00
	Anatomy of the Abdomen	Arranged, part time	150.00
	Applied Anatomy for the Otolaryngologist	Arranged, 150 hours, part time	275.00
	Applied Anatomy of the Urogenital System	Arranged, 130 hours, part time	300.00
	Applied Anatomy for the Anesthetist	Arranged, 125 hours, part time	275.00
	Anatomy for the Orthopedic Surgeon	Arranged, 100 hours, part time	150.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, New York	Anatomy, Dissections, Demonstrations and Lectures	Arranged, part time	200.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	411-A Anatomy of the Head and Neck	September 28-December 18, 3 days a week, part time	90.00
	412-A Anatomy of the Thorax and Its Viscera	January 4-March 26, 3 days a week, part time	90.00
	413-A Anatomy of the Abdomen	September 28-December 18, 3 days a week, part time	90.00
	414-A Anatomy of the Female Pelvis	January 4-March 26, 3 days a week, part time	90.00
Western Reserve University School of Medicine, 2109 Adelbert Rd., Cleveland 6, Ohio	Anatomy 11-G	October 1-April 30, arranged, 5 days, part time	75.00
Hillcrest Medical Center, Twelfth St. and Utica Ave., Tulsa, Okla.	Anatomy	Arranged, once weekly, part time	None
	ANESTHESIOLOGY		
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Anesthesiology	4 months, intervals of 2 months, full time	300.00
University of Southern California School of Medicine, 3551 University Ave., Los Angeles, Calif. At: Los Angeles County General Hospital	#892 "Anesthesia"	September 2-December 2, full time	300.00
American Society of Anesthesiologists, Inc., 188 W. Randolph St., Chicago, Ill.[95] At: St. Francis Hospital, Hartford, Conn.	Anesthesiology: Regional and General	July, October and January, 3 months, full time	None

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Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	ANESTHESIOLOGY—Continued		
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Practical Course in Endotracheal Anesthesia	Arranged, 2 weeks, full time	$150.00
	Practical Course in Ether, Nitrous Oxide, Ethylene and Cyclopropane Anesthesia	Arranged, 1 month, full time	200.00
	Practical Course in Nitrous Oxide and Ether Anesthesia	Arranged, 1 month, full time	125.00
	Practice Course in Spinal and Intravenous Anesthesia	Arranged, 2 weeks, full time	150.00
University of Buffalo School of Medicine, 24 High St., Buffalo, N. Y.	Anesthesia	October 7, 14, 21, 28-November 4, 11, 18, 25-December 2 and 9, 10 half days	50.00
	Anesthesia	November 9-13, full time	50.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Clinical Anesthesiology	Arranged, 3 months, full time	200.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Applied Anesthesia	October and January, 3 months, full time	300.00
	Anesthetic Technic	October and January, 6 weeks, full time	100.00
	Regional and Spinal Anesthesia	October and January, 6 weeks, full time	100.00
New York State Society of Anesthesiologists, 137 W. 11th St., New York 11, N. Y. At: Various hospitals in New York City	Postgraduate Training in Anesthesiology	Arranged, continuously throughout year	None
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	510-A Anesthesiology: Endotracheal and Related Methods	August 31-September 15, part time	75.00
	511-A Anesthesiology (for Specialists)	Arranged, September-June, 2 weeks, full time	150.00
	512-A Regional Anesthesiology	January 4-January 16, full time	200.00
	513-A Anesthesiology (Graduate Course)	Arranged, after September 8, 1 year, full time	700.00
	514-A	September 14-December 5, part time	200.00
	ARTHRITIS		
Tufts College Medical School, Postgraduate Division, 30 Bennet St., Boston, Mass.[2] At: New England Medical Center	Rheumatic Diseases	December 14-16, full time	30.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Arthritis	Arranged, 8 weeks, once weekly	50.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5414-A Arthritis and Allied Rheumatic Disorders	July 6-10, full time	75.00
	5414-B Arthritis and Allied Rheumatic Disorders	November 9-13, full time	75.00
	BACTERIOLOGY		
Public Health Service, Communicable Disease Center, Atlanta, Ga.	Laboratory Diagnosis of Bacterial Diseases, Part 1, General Bacteriology	September 21-October 2, full time	None
	Laboratory Diagnosis of Bacterial Diseases, Part 2, General Bacteriology	October 5-16, full time	None
	Laboratory Diagnosis of Parasitic Diseases, Part 1, Intestinal Parasites	September 21-October 16, full time	None
	Laboratory Diagnosis of Parasitic Diseases, Part 2, Blood Parasites	October 19-November 6, full time	None
	Laboratory Diagnosis of Bacterial Diseases, Enteric Bacteriology	October 19-30, full time	None
	Laboratory Diagnosis of Bacterial Diseases	November 2-6, full time	None
	Laboratory Diagnosis of Rabies	November 9-13, full time	None
	Laboratory Diagnosis of Parasitic Diseases	November 16-20, full time	None
	Laboratory Methods in Medical Mycology	November 23-27, full time	None
At: Montgomery, Ala.	Laboratory Diagnosis of Virus Diseases	October 19-30, full time	None
University of Michigan Medical School, Ann Arbor, Mich.	Basic Sciences (Bacteriology)	December 7-18, full time	250.00
Wayne University College of Medicine, 1512 St. Antoine, Detroit, Mich.	Microbiology Seminar	September 14-December 5, December 7-March 13, once weekly, part time	15.00
	Virology	September 14-December 5, 12 weeks, 3 times weekly, part time	50.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Bacteriology	Arranged, monthly, part time	100.00
	Immunology	Arranged, 6 weeks, part time	50.00
	Parasitology	Arranged, 6 weeks, part time	75.00
	BASIC SCIENCE		
University of Southern California, Division of Graduate Medicine, 1200 N. State St., Los Angeles, Calif.	#820 Basic Science	Arranged	Contract
University of Maryland School of Medicine, 29 S. Greene St., Baltimore, Md.	Formal Basic Science Course	October-June, once weekly, part time	50.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Basic Sciences [47]	October, 9 months, full time	710.00 [46]
University of Pennsylvania, Graduate School of Medicine, Philadelphia 4, Pa.	Basic Medical Sciences	September 28-May 22, full time	960.00
University of South Dakota, School of Medical Sciences, Vermillion, S. D.	Postgraduate Basic Science [48]	September 1-January 19, part time	75.00
University of Puerto Rico, School of Medicine, San Juan 22, P. R.	Seminar in Basic Sciences for Hospital Residents	Arranged, 3 years, once weekly, part time	Not given
	BIOCHEMISTRY		
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: Beth El Hospital	Clinical Biochemistry	October, 10 weeks, once weekly, part time	30.00

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Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
CARDIOVASCULAR DISEASES			
Department of the Army, Office of the Surgeon General, Washington 25, D. C. At: Fitzsimons Army Hospital, Denver, Colo.	Clinical Electrocardiography and Recent Advances in Cardiovascular Diseases	November 9-14, 11 sessions, full time	None [49,50,51]
Delaware Academy of General Practice, 1305 New Rd., Wilmington 5, Del. At: Delaware Academy of Medicine	Cardiology for the General Practitioner	Once weekly, 8 weeks, part time	$55.00 non-members
Chicago Medical Society, 86 E. Randolph St., Chicago, Ill. At: Sheraton Hotel	Cardiology and Hematology	November 9-13, full time	75.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Personal Course in Cardiovascular Disease	September 23, 10 days, part time	100.00
Maryland Academy of General Practice, 4215 Park Heights Ave., Baltimore, Md.[3] At: National Institutes of Health, Bethesda	Cardiac Symposium	May 14, 1 day, full time	None
Harvard Medical School, Courses for Graduates, 25 Shattuck St., Boston, Mass. At: Beth Israel Hospital	Cardiology 1	January 25-May 7, full time	505.00
At: Boston City Hospital	Cardiology 2	November 4-January 27, Wednesday mornings, part time	780.00
At: Peter Bent Brigham Hospital	Clinical Heart Disease	July 1-31, full time	205.00
At: Massachusetts General Hospital	Cardiovascular Disease	October 1-September 30, full time	805.00
University of Minnesota, Center for Continuation Study, Minneapolis 14, Minn.[4]	Symposium on Cardiovascular Physiology and Surgery	September 14-16, full time	None
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: Jewish Sanitarium and Hospital for Chronic Disease	Advances in Cardiology and Electrocardiography	October, 10 weeks, once weekly, part time	30.00
	Clinical Ballistocardiography	October, 8 weeks, once weekly, part time	20.00
At: Coney Island Hospital	Cardiovascular Disease	October, 10 weeks, once weekly, part time	20.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Mount Sinai Hospital	Medicine PM 29 Clinical Cardiology	October 13-December 15, once weekly, part time	45.00
	Medicine PM 31 Cardiovascular Diseases	November 2-13, January 18-29, full time	140.00
	Medicine PM 60 Cardiology I	September 24-June 3, once weekly, part time	300.00
	Medicine PM 62 Cardiology II Section A	September 22-January 26, once weekly, part time	150.00
	Medicine PM 63 Cardiology III Section A	September 22-January 26, once weekly, part time	200.00
	Medicine PM 64 Recent Advances in Diagnosis and Treatment of Heart Disease	September 21-January 25, once weekly, part time	150.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Cardiology	September-June, 20 weeks, part time	150.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Electrocardiographic Interpretation	Arranged, 2 weeks, part time	75.00
	Diagnosis and Treatment of Diseases of the Heart	Arranged, 3 weeks, part time	75.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5427-A Auscultation of the Heart	September 14-16, full time	50.00
	5428-A Cardiac Roentgenology	September 17 and 18, full time	30.00
	5431-A Modern Concepts in Etiology Diagnosis and Treatment of Heart Disease	January 11-15, full time	50.00
St. Francis Sanatorium for Cardiac Children, Roslyn, N. Y.	A Course of Seminars on Heart Diseases in Children	October-May, once monthly, part time	None
North Carolina Board of Health, Raleigh, N. C. At: Duke University School of Medicine	Refresher Course in Cardiology	July and December, 3 days, full time	Not given
Cleveland Area Heart Society, 2073 E. 9th St., Cleveland 15, Ohio At: Western Reserve University School of Medicine	Cardiac Resuscitation Course	August-June, 2 days, once monthly, full time	20.00 [53]
Albert Einstein Medical Center, Northern Division, York and Tabor Rds., Philadelphia 41, Pa.	Postgraduate Course in Cardiology	Arranged, 12 weeks, part time	50.00
Hahnemann Medical College and Hospital, 230 N. Broad St., Philadelphia, Pa. At: Hahnemann Hospital	Postgraduate Cardiology Course	October-May, once weekly, part time	100.00
	Advanced Cardiology Course	October-May, once weekly, part time	200.00
Vermont Heart Association Health Commission, University of Vermont College of Medicine, Pearl St., College Park, Burlington, Vt. At: University of Vermont College of Medicine	Cardiovascular Disease	October 6-10, full time	Not given
	Cardiovascular Disease	October 19-23, full time	None
Kanawha Medical Society, 310 Atlas Building, Charleston 1, W. Va.	Recent Advances in Cardiac Therapy	September 16, full time	None
DERMATOLOGY AND SYPHILOLOGY			
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Dermatology	January 6-March 24, once weekly, part time	40.00
University of California Medical Extension, 10851 LeConte Ave., Los Angeles 24, Calif. At: Veterans Administration Hospital	Dermatology for General Practitioners	October 7-November 11, once weekly part time	30.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Clinical Refresher Course in Dermatology	Arranged, 2 or more weeks, full time	75.00 (2 weeks)
	Clinical Course in Dermatology	Arranged, 1 year, full time	1,000.00
	Intensive Course in Dermatology	Arranged, 2 weeks, full time	100.00
Harvard Medical School, Courses for Graduates, 25 Shattuck St., Boston, Mass. At: Massachusetts General Hospital	Dermatology and Syphilology 1	October 1-September 30, full time	805.00
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich.	Dermapathology	December 7-March 13, 12 weeks, once weekly, part time	50.00
At: Receiving Hospital	Seminar in Dermatology	September 14-December 5, December 7-March 13, 12 weeks, once weekly	15.00
	Dermapathology Seminar	September 14-December 5, 12 weeks, once weekly, part time	15.00
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.	Dermatology for General Physicians	November 19-21, full time	25.00

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Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
DERMATOLOGY AND SYPHILOLOGY—Continued			
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: Kings County Hospital	Dermatology for the General Practitioner	October, 8 weeks, once weekly, part time	$20.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Columbia Presbyterian Medical Center	Dermatology GM 1 Clinical Dermatology	July 1, 6 months, full time	230.00
	Dermatology GM 1 Clinical Dermatology	July 1, 12 months, full time	460.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Dermatology and Syphilology for the general Practitioner (Seminar)	Arranged, 5 days	75.00
	Dermatology and Syphilology for Specialists (Seminar)	Arranged, 5 days	75.00
	Dermatologic Histopathology (Seminar)	Arranged, 5 days	75.00
	Training for Specialization in Dermatology and Syphilology	3 years, full time	1,000.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	521-A A Comprehensive Review in Dermatological Histopathology	Arranged, 5 days, full time	75.00
	524-A Dermatology and Syphilology (Designed for Pediatricians)	September 21-25, full time	75.00
	525-A Dermatology and Syphilology (Postgraduate Course)	October 1-September 30, full time	700.00
	Short term and Practical Courses in Dermatology and Syphilology	Arranged, 1 week to 12 months, full time	125.00 per month
American College of Physicians, 4200 Pine St., Philadelphia, Pa. At: New York University College of Medicine, New York, N. Y.	Cardiovascular Diseases [95]	October 12-17, full time	30.00 members 60.00 non-members
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Dermatology and Syphilology [48]	September 28-May 22, full time	960.00
DIABETES			
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	General Management of Diabetes Mellitus	October 1-December 10, once weekly part time	60.00
University of Oregon Medical School, 3181 S. W. Sam Jackson Park Rd., Portland 1, Ore.	Diabetes and Metabolism	November 9-11, full time	30.00
ELECTROCARDIOGRAPHY			
University of California Medical Extension, 10851 LeConte Ave., Los Angeles 24, Calif. At: University of California	Electrocardiography	Twice weekly, 3 weeks, part time	20.00
University of Southern California, Division of Graduate Medicine, 1200 N. State St., Los Angeles, Calif. At: Los Angeles County Hospital	#880 Electrodiagnosis and Electromyography	3 months, arranged, full time	100.00
Department of the Army, Office of the Surgeon General, Washington 25, D. C. At: Fitzsimons Army Hospital, Denver, Colo.	Clinical Electrocardiography and Recent Advances in Cardiovascular Diseases	November 9-14, 11 sessions, full time	None [49,50,51]
Mount Sinai Hospital, 4300 Alton Road, Miami Beach, Fla.	Introduction to Clinical Electrocardiography (ECG I)	September 28-December 16, twice weekly, part time	25.00
	Interpretation of the Electrocardiogram (ECG II)	October 6-December 10, twice weekly, part time	30.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Intensive Course in Electrocardiography and Heart Disease	July 13 and September 28, 2 weeks, full time	150.00
	Personal Course in Electrocardiography and Heart Disease	October 14, 10 days, part time	150.00
Michael Reese Hospital Postgraduate School, 29th St. and Ellis Ave., Chicago, Ill.	Electrocardiographic Interpretation	August 3-15, full time	150.00
Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, La.	Electrocardiography	November 30-December 11, full time	100.00
Beth Israel Hospital, 330 Brookline Ave., Boston, Mass.	Practical Electrocardiography Course A	November 9-13, full time	100.00
	Practical Electrocardiography Course B	October, November and December, 10 Wednesday afternoons, part time	100.00
Tufts College Medical School, Postgraduate Division, 30 Bennet St., Boston, Mass. At: New England Center Hospital	Electrocardiography I	November 30-December 4, full time	45.00
	Electrocardiography II	January 11-13, full time	30.00
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: Jewish Hospital	Electrocardiography for the General Practitioner	October, 6 weeks, three days a week, part time	30.00
At: Beth El Hospital	Basic Electrocardiography	October, 6 weeks, twice weekly, part time	20.00
University of Buffalo School of Medicine, 24 High St., Buffalo, N. Y.	Electrocardiography in Clinical Practice	September 24, October 1, 8, 15, 22, 29-November 5, 12, 19, 9 half days	50.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Mount Sinai Hospital	Medicine PM 41 Intensive Course in Elementary Electrocardiography	October 19-24, January 4-10, full time	60.00
	Medicine PM 42 Intensive Course in Advanced Electrocardiography	October 26-31, January 11-16, full time	60.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Electrocardiography	Arranged, fall and spring, 2 weeks, part time	100.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5423-A Electrocardiography	November 16-20, full time	75.00
Hillcrest Medical Center, Twelfth St. and Utica Ave., Tulsa, Okla.	Postgraduate Study Course	Fall, six weeks, once weekly, full time	None
ELECTROENCEPHALOGRAPHY			
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Columbia Presbyterian Medical Center	Neurology PM 2 Clinical Electroencephalography and Electromyography	October 1-January 2, full time	250.00
	Neurology PM 33 Clinical Electroencephalography	October 1-January 14, once weekly, part time	60.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	642-A Electroencephalography	Arranged, 8 weeks, part time	300.00

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Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	ENDOCRINOLOGY		
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.[5]	Postgraduate Assembly in Endocrinology	September 28-October 3, full time	Not given
University of Nebraska College of Medicine, 42nd St. and Dewey Ave., Omaha, Neb.[6]	Recent Advances in Endocrinology	September 22-24, full time	$15.00
Joint Committee on Postgraduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1]			
At: Kings County Hospital	Metabolic Endocrinology	October, 12 weeks, once weekly, part time	20.00
At: Jewish Hospital	Medical and Gynecologic Endocrinology	October, 10 weeks, once weekly, part time	20.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Endocrinology	Arranged, fall, 2 weeks, part time	100.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5422-A Endocrinology	November 16-20, full time	50.00
Endocrine Society, 1200 N. Walker St., Oklahoma City, Okla.[7]	Postgraduate Assembly in Endocrinology and Metabolism	September 28-October 3, full time	125.00
	ENDOSCOPY		
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Course in Bronchoscopy	Arranged, 1 week, full time	100.00
	Practical Course in Cystoscopy	10 days, full time [54]	150.00
	Clinical Bronchoscopy	September 23, 8 days, part time	150.00
University of Illinois College of Medicine, Department of Otolaryngology, 1853 W. Polk St., Chicago 12, Ill.	Bronchoesophagology	October or November, 2 weeks, full time	150.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y.			
At: Columbia Presbyterian Medical Center	Otolaryngology PM 1 Bronchoscopy	October 5-23, full time	250.00
	Medicine PM 2 Gastroscopy	Arranged, 2 months, 3 times a week, part time	250.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Gastroscopy	Arranged, 2 weeks, part time	200.00
	Gastroscopy (Advanced)	Arranged, 5 weeks, part time	200.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Bronchoscopy	Arranged, 4 weeks, part time	150.00
Temple University School of Medicine, 3400 N. Broad St., Philadelphia 40, Pa.	Postgraduate Course in Bronchoesophagology	September 21-October 2, full time	250.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa	Bronchoesophagology, Gastroscopy and Laryngeal Surgery	September 14-26, full time	250.00
	Bronchoesophagology, Gastroscopy and Laryngeal Surgery	First two weeks in January, full time	250.00
	FRACTURES		
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Intensive Course in Fractures and Traumatic Surgery	October 26, 2 weeks, full time	150.00
	Clinical Course in Fractures	Arranged, 1 or 2 weeks, full time	50.00 1 week
	Special Course in Fractures	September 23, 10 days, part time	125.00
State University of Iowa College of Medicine, Iowa City, Iowa			
At: University Hospital	Acute Trauma and Fractures	September 18-19, full time	5.00
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.	Fractures for General Physicians	November 16-18, full time	25.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	6611-A Pitfalls in the Internal Fixation of Fractures	November 9-14, full time	90.00
	GASTROENTEROLOGY		
University of Southern California, Division of Graduate Medicine, 1200 N. State St., Los Angeles, Calif.			
At: Los Angeles County Hospital	‡844 Gastroenterology	1 year, September, full time	1,000.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Personal Course in Gastroscopy and Gastroenterology	September 14 and November 2, 2 weeks, full time	200.00
	Course in Gastroenterology	October 26, 2 weeks, full time	100.00
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich.			
At: Receiving Hospital	Gastroenterology	September 14-December 5, December 7-March 13, 12 weeks, once weekly part time	15.00
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1]			
At: Jewish Hospital	Gastroscopy	October, 5 weeks, once weekly, part time	20.00
At: Greenpoint Hospital	Gastroenterology	October, 8 weeks, twice weekly, part time	30.00
At: Cumberland Hospital	Gastroenterology	October, 6 weeks, twice weekly, part time	30.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y.			
At: Montefiore Hospital	Medicine PM 70 Gastroenterology	September 15-December 29, once weekly, part time	75.00
	Medicine PM 73 Advanced Gastroenterology	January 19-May 11, once weekly, part time	75.00
National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.			
At: Hotel Biltmore, Los Angeles, Calif.	Postgraduate Gastroenterology	October 15-17, full time	35.00 members 50.00 non-members
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Gastroenterology	Arranged, fall and winter, 1 month part time	100.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Clinical Gastroenterology	Arranged, 6 weeks, part time	75.00
	Proctology, Gastroenterology, Operative Proctology (Dissection)	October and January, 6 weeks, part time	200.00
	Clinical Proctology and Gastroenterology	October and January, 6 weeks, part time	100.00
	Clinical Proctology	Arranged, 6 weeks, part time	75.00
	Clinical and Cadaver Proctology	Arranged, 6 weeks, part time	175.00
	Clinical Gastroenterology	Arranged, 6 weeks, part time	75.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5421-A Gastroenterology	October 12-16, full time	45.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Gastroenterology [48]	September 28-May 22, full time	900.00
	GERIATRICS		
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5426-A Geriatrics	July 20-22, full time	30.00

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	HEMATOLOGY		
Chicago Medical Society, 86 E. Randolph St., Chicago, Ill. At: Sheraton Hotel	Cardiology and Hematology	November 9-13, full time	$75.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Personal Course in Morphologic Hematology	September 23, 10 days, part time	150.00
Michael Reese Hospital, 29th St. and Ellis Ave., Chicago, Ill.	Hematologic Diagnosis and Treatment of Blood Dyscrasias	July 20-August 1, full time	150.00
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich.	Beginning Hematology	September 14-December 5, 12 weeks, once weekly, part time	50.00
	Advanced Hematology	December 7-March 13, 12 weeks, once weekly, part time	50.00
	Review of Clinical Hematology	September 14-December 5, 12 weeks, once weekly, part time	15.00
At: Receiving Hospital	Hematology Clinic	September 14-December 5, 12 weeks, once weekly, part time	15.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y.			
At: Mount Sinai Hospital	Medicine PM 35 Hematology	November 3-December 22, once weekly, part time	50.00
	Medicine PM 66 Clinical Hematology	September 15-January 19, once weekly, part time	75.00
	Medicine PM 67 Advanced Hematology	September 22-January 5, once weekly, part time	75.00
New York Academy of Medicine, Committee on Medical Education, 2 East 103rd St., New York 29, N. Y.	Disorders of the Blood and the Blood-Forming Organs	October 19-30, full time	10.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Hematology	Arranged, 2 months, part time	50.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa. At: Bryn Mawr Hospital, Bryn Mawr, Pa.	Clinical and Laboratory Hematology	October and December, 6 weeks, full time	200.00
At: Children's Hospital	Practical Pediatric Hematology	September 15-17, full time	60.00
	HOSPITAL ADMINISTRATION		
Albert Einstein Medical Center, Northern Division, York and Tabor Rds., Philadelphia 41, Pa.	Postgraduate Hospital Training Program	Arranged, 20 weeks, once weekly, part time	35.00
University of Pittsburgh Graduate School of Public Health, Pittsburgh 13, Pa.	Public Health Practice, Occupational Health and Hospital Administration	September-June, full time	700.00
	INDUSTRIAL MEDICINE		
University of Michigan School of Public Health, Ann Arbor, Mich.[8]	Fifth Industrial Health Discussional (Seminar)	December 11-12, full time	Not given
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	480-A Introduction to Radiological Safety	Fall, 2 weeks, full time	50.00
	481-A Industrial Medicine (Graduate Course)	September 28, 1 year, full time	700.00
University of Cincinnati, Institute of Industrial Health, Eden and Bethesda Aves., Cincinnati 19, Ohio [9]			
At: Kettering Laboratory	915, 916—Kettering Laboratory Seminar	September-May, once weekly, part time	Arranged
	Occupational Skin Problems [55]	October 12-16, full time	50.00
	Industrial Medicine	July 1, 12 months, full time	400.00
	960 Medicolegal Aspects of Industrial Medicine	January-May, twice weekly, part time	Arranged
	911, 912—Industrial Physiology [55]	September-May, twice weekly, part time	Arranged
	Industrial Medicine	July 1, 3 years, full time	Fellowship Stipend
University of Pittsburgh Graduate School of Public Health, Pittsburgh 13, Pa.	Public Health Practice, Occupational Health, and Hospital Administration	September-June, full time	700.00
	INTERNAL MEDICINE		
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Basic Science in Internal Medicine [55]	September 28-June 4, full time	800.00
	Surgical Diseases of the Peripheral Vascular System	January 5-February 23, once weekly, part time	30.00
At: Los Angeles County General Hospital	Differential Diagnosis of Internal Diseases	January 5-February 23, once weekly, part time	30.00
University of Southern California, Division of Graduate Medicine, 1200 N. State St., Los Angeles, Calif.			
At: Los Angeles County Hospital	‡830 Internal Medicine	1 year, September, full time	1,000.00
	‡855 Intensive Review of Internal Medicine	September 14-25, part time	50.00
University of Colorado Medical Center, 4200 E. Ninth Ave., Denver 20, Colo.	Recent Advances in Infectious Diseases	July, 4 days, full time	40.00
Georgetown University School of Medicine, 3900 Reservoir Rd., N. W., Washington, D. C.	Internal Medicine	Arranged, 15 weeks, part time	75.00
Emory University School of Medicine, 36 Butler St., S. E., Atlanta, Ga. At: Grady Memorial Hospital	General Internal Medicine	Arranged, 2 weeks-12 months, full time	[56]
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Intensive Course in Internal Medicine	October 12, 2 weeks, full time	125.00
Iowa Academy of General Practice, 912 Equitable Bldg., Des Moines, Iowa At: Hotel Savery	Peripheral Vascular Disease	September 24, 1 day, full time	Non-members 5.00 members free
University of Kansas Medical Center, 39th St. and Rainbow Blvd., Kansas City, Kan.[10]	Internal Medicine	November 16-19, full time	40.00
Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, La.	Internal Medicine for General Practitioners	March 22-27, full time	50.00
Harvard Medical School, Courses for Graduates, 25 Shattuck St., Boston, Mass. At: New England Deaconess Hospital	Diabetes and Endocrinology in Relation to General Medicine	July 6-8, full time	35.00
At: Boston City Hospital	Internal Medicine 1	September 1-August 31, full time	605.00
	Internal Medicine 2	September 1-November 28, full time	380.00

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Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
INTERNAL MEDICINE—Continued			
Tufts College Medical School, Postgraduate Division, 30 Bennet St., Boston, Mass. At: New England Medical Center	Review of Recent Advances in Internal Medicine	October 5-10, full time	$55.00
University of Michigan Medical School, Ann Arbor, Mich. At: University Hospital	Clinical Internal Medicine	October-May, 1 day weekly, full time	65.00
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich. At: Receiving Hospital	Medical Conference	September 14-December 5, December 7-March 13, 12 weeks, once weekly, part time	15.00
	Medical X-Ray Conference	September 14-December 5, December 7-March 13, 12 weeks, once weekly, part time	15.00
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: Jewish Hospital	Internal Medicine	October, 8 weeks, once weekly, part time	20.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Internal Medicine	August-June, 1 month, full time	150.00
	Internal Medicine	August-June, 2 months, full time	300.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Surgical Aspects of Peripheral Vascular Diseases	Arranged, part time	200.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5429-A Internal Medicine (Graduate Course)	September 28, 1 year, full time	700.00
	5418-A Peripheral Vascular Disease	November 30-December 4, full time	50.00
	5424-A Nephritis and Hypertension	July 13-17, full time	50.00
	5424-A Nephritis and Hypertension	October 26-30, full time	50.00
American College of Physicians, 4200 Pine St., Philadelphia, Pa. At: University of Chicago School of Medicine, Chicago, Ill.	Internal Medicine [95]	October 19-23, full time	30.00 members 60.00 non-members
At: Vanderbilt University School of Medicine, Nashville, Tenn.	Seminars in Internal Medicine [95]	October 19-23, full time	30.00 members 60.00 non-members
At: Duke University School of Medicine, Durham, N. C.	Physiological Basis of Internal Medicine [95]	October 12-16, full time	30.00 members 60.00 non-members
At: University of Wisconsin Medical School	The Newer Biological and Physiological Approaches to Clinical Problems [95]	November 16-20, full time	30.00 members 60.00 non-members
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Internal Medicine [48]	September 28-May 22, full time	960.00
LEGAL MEDICINE			
School of Public Health, University of Michigan, Ann Arbor, Mich.[11]	Seminar — Technical Testimony Involving Medical and Health Problems	October 21, 1 day, full time	10.00
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.	Medical Jurisprudence for General Physicians	November 5 and 6, full time	20.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	531-A Forensic Medicine (Graduate Course)	September 28-June 18, full time and part time	700.00
	532-A Forensic Medicine	Arranged	100.00 a month
MALIGNANT DISEASE			
Colorado State Medical Society, 835 Republic Building, Denver, Colo.[12]	Cancer Conference	July 8-9, full time	None
Dade County Cancer Institute, Cancer Cytology Center, 1155 N. W. 14th St., Miami, Fla.	Seminar for Physicians on Techniques and Procedures in Cancer Cytology	October, 1 day, full time	Not given
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Columbia Presbyterian Medical Center	Cancer PM 1 Cancer Diagnosis and Treatment	November 16-28, full time	100.00
University of Oregon Medical School, 3181 S. W. Sam Jackson Park Rd., Portland 1, Ore.[13]	Diagnosis and Treatment of Malignant Neoplasms	September 14-18, full time	25.00 [57]
MEDICAL TECHNOLOGY			
University of Kansas Medical Center, 39th St. and Rainbow Blvd., Kansas City, Kan.[10]	Medical Technology	January 11-13, full time	10.00
MEDICINE, GENERAL			
Alabama Academy of General Practice, 17 Molton St., Montgomery, Ala. At: Medical College of Alabama	Alabama Academy Postgraduate Seminar	August, 2 days, full time	None
Medical College of Alabama, 620 S. 20th St., Birmingham, Ala. At: St. Jude's Hospital, Montgomery	Central Alabama Postgraduate Assembly	Semi-monthly, second and fourth Tuesday, part time	3.00 per session
At: Selma	Black Belt Postgraduate Assembly	Bi-monthly, third Thursday, part time	Not given
University of Arkansas School of Medicine, 1209 McAlmont St., Little Rock, Ark.[14]	Arkansas Postgraduate Program	1-3 days during academic year, full time	None
Los Angeles County Medical Association, 814 Pine Ave., Long Beach, Calif. At: Veterans Administration Hospital	Postgraduate Seminar	October-November, 8 weeks, part time	25.00
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	General Medicine	September 29-December 15, once weekly, part time	50.00
University of California, Medical Extension, 10851 LeConte Ave., Los Angeles 24, Calif. At: University of California	Annual Evening Lecture Course	September-December, 12 weeks, part time	50.00

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Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
MEDICINE, GENERAL—Continued			
California Academy of General Practice, 461 Market St., San Francisco, Calif. At: Hotel del Coronado	1953 Scientific Assembly	October 25-27, full time	$5.00 non-members free to members
University of California School of Medicine (Medical Extension), Medical Center, San Francisco, Calif. At: Mills Memorial Hospital, San Mateo At: East Oakland Hospital	Evening Lectures in Medicine Medicine for General Practitioners	Fall, weekly, 12 weeks, part time Fall, weekly, 12 weeks, part time	Not given 50.00
San Diego County General Hospital, San Diego, Calif.	Annual Postgraduate Assembly	September 23-24, full time	None
San Diego County Medical Society, San Diego, Calif. At: Mercy Hospital, San Diego	Recent Advances in Medicine	Once weekly for twelve weeks, part time	50.00 [58]
Saint John's Hospital, Santa Monica, Calif.	Annual Postgraduate Assembly	September, 3 days, full time	10.00
California Medical Association, 1036 N. Center St., Stockton, Calif.	Circuit Postgraduate Lectures for the North Coast Counties Circuit Postgraduate Lectures for Sacramento Valley Counties	September-October, 8 weeks, part time September-October, 8 weeks, part time	25.00 25.00
San Joaquin County Medical Society, 2633 Pacific Ave., Stockton, Calif. At: Stockton State Hospital	Stockton Postgraduate Study Club	Fall, once weekly, 8 weeks	10.00
Yale University School of Medicine, 333 Cedar St., New Haven, Conn.[15]	Connecticut Clinical Congress	September 16-17, full time	2.00
Delaware Academy of General Practice, 1305 New Rd., Wilmington 5, Del. At: Delaware Academy of Medicine	Second Annual Scientific Session (General Medicine)	December 12, 1 day, full time	None
Medical Society of the District of Columbia, 1718 M St., N. W., Washington, D. C. At: Hotel Statler	24th Annual Scientific Assembly	October 5-7, full time	3.00 for non-members [59]
Emory University School of Medicine, 36 Butler St., S. E., Atlanta, Ga.[16] At: Grady Memorial Hospital	Postgraduate Course for General Practitioners	October 5-9, full time	10.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Intensive Personal Course in Liver and Biliary Tract Diseases Personal Course in General Medicine	September 21, 1 week, full time September 23, 10 days, part time	100.00 100.00
Illinois Academy of General Practice, 14 E. Jackson Blvd., Chicago, Ill.[17] At: Alton, Belleville, Chicago, Danville, Elmhurst, Herrin, Joliet, Moline, Peoria, Rockford, Springfield, Decatur and Effingham	Medicine for Today—Weekly Integrated Lectures	October 13-November 20, 2 days each center, part time	40.00 members 75.00 non-members
Boston University School of Medicine, 80 E. Concord St., Boston 18, Mass. At: Massachusetts Memorial Hospitals	Postgraduate Course in Medicine	November 4-April 28, part time	100.00
Postgraduate Medical Institute, 22 The Fenway, Boston 15, Mass.[18] At: Throughout the State	Courses in General Medicine	October through April	Not given
Michigan State and Wayne County Academies of General Practice, 15125 Grand River, Detroit 27, Mich.[19] At: Kellogg Center, East Lansing	Annual Fall Postgraduate Clinic	November 11-12, full time	5.00 non-members
University of Michigan Medical School, Ann Aror, Mich.	Clinical Exercises for Practitioners	October, November, December, 1 day weekly, full time	25.00
At: Alpena, Battle Creek, Bay City, Cadillac, Flint, Jackson, Lansing, Mt. Clemens, Muskegon, Traverse City, Escanaba, Houghton, Iron Mountain, Ironwood, Marquette, and Sault Ste. Marie	Extramural Course	1 day in each center in fall, 1 day in spring, full time	None
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.	Dental Problems in Medicine for Physicians	October 21, one day, full time	10.00
Mississippi Academy of General Practice [60] At: Heidelberg Hotel, Jackson, Miss.	General Seminar	December 10, 1 day, full time	None
Kansas City Southwest Clinical Society, 3036 Gillham Rd., Kansas City 8, Mo. At: Municipal Auditorium	Annual Fall Clinical Conference	September 28-October 1, full time	20.00
Nebraska State Medical Association, 1315 Sharp Bldg., Lincoln, Neb.[20] At: Scotts Bluff, North Platte, McCook, Grand Island, Norfolk and Beatrice	Regional Postgraduate Course (Circuit)	September, tentative, part time	None
Omaha Mid-West Clinical Society, 1031 Medical Arts Bldg., Omaha 2, Neb. At: Hotel Paxton	Annual Postgraduate Clinical Assembly	October 26-30, part time	7.00 [61]
Atlantic City Hospital, 20 S. Ohio Ave., Atlantic City, N. J.	Visiting Chief Program	50 weeks, continuous, part time	None
Academy of Medicine of New Jersey, 91 Lincoln Park, Newark, N. J.	Fourth Graduate Week of the Academy of Medicine of New Jersey	November 16-20, full time	None
New Mexico Academy of General Practice, 301 W. Tilden St., Roswell, N. Mex. At: Throughout the State	Circuit Courses	Fall, 1 day, full time	Not given
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: Kings County Hospital	Recent Progress in Internal Medicine	October, 10 weeks, once weekly, part time	30.00
At: St. John's Episcopal Hospital	Modern Chemotherapy in Clinical Practice	October, 5 weeks, once weekly, part time	20.00
At: Jewish Hospital	Hypertension and Nephritis	October, 8 weeks, once weekly, part time	20.00
University of Buffalo School of Medicine, 24 High St., Buffalo, N. Y.	Annual Postgraduate Course for Physicians	September 14-19, full time	50.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Mount Sinai Hospital	Medicine PM 30 Present Day Methods in Medical Practice Medicine PM 65 Peripheral Vascular Diseases Medicine PM 72 Neoplastic Diseases	October 12-17, full time September 24-April 1, once weekly, part time September 15-January 26, once weekly, part time	75.00 125.00 150.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	General Medicine General Practitioner's Course	Arranged, 4 weeks, full time Arranged, 4 weeks, full time	100.00 100.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5430-A Review Course in General Medicine	July 13-24, full time	100.00

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Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
MEDICINE, GENERAL—Continued			
Duke University School of Medicine, Durham, N. C.	Postgraduate Seminar	October or November, 3 days, full time	Not given
Medical Society of the State of North Carolina, 203 Capitol Club Building, Raleigh, N. C. At: Two local communities in the state	Postgraduate Lecture Series	October and November, 4 weeks, once weekly, part time	$20.00
New Hanover Medical Society, Wilmington, N. C. At: Wrightsville Beach, Wrightsville Beach, N. C.	New Hanover Medical Symposium	August, 1 day, full time	Not given
North Carolina Academy of General Practice, 817 Nissen Building, Winston-Salem, N. C.[21] At: University of North Carolina School of Medicine	Annual Scientific Assembly	October 18-20, full time	None
Oklahoma City Clinical Society, 512 Medical Arts Bldg., Oklahoma City, Okla. At: Biltmore Hotel	Clinical Conference	October, 4 days, full time	20.00
Hillcrest Medical Center, Twelfth St. and Utica Ave., Tulsa, Okla.	Medicine [62]	Arranged, once weekly, part time	None
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa. At: Graduate Hospital and private offices	Advances in Medicine and Surgery	September 21-25, full time	[63]
	Segmental Neuralgias; Relief by Regional Anesthesia [64]	October-May, arranged, 3 weeks, full time	200.00
Medical College of South Carolina, 16 Lucas St., Charleston, S. C.[22]	Postgraduate Seminar	November 3-5, full time	5.00
Piedmont Post-Graduate Clinical Assembly, The Clemson House, Clemson, S. C. At: Anderson County Hospital, Anderson	Piedmont Postgraduate Clinical Assembly	September 17-18, part time	7.50
South Carolina Academy of General Practice, Clemson House, Clemson, S. C. At: Different localities in State	Scientific Assembly	August, 2 days	Not given
University of South Dakota, School of Medical Sciences, Vermillion, S. D.	Master of Medical Science [65]	July 1 and September 1, 1 year, full time	100.00
Andrew Jackson Academy of General Practice, 217 N. Main St., Dickson, Tenn. At: Nashville or adjacent towns	Continuation Course in General Practice	August, October and December, once weekly, part time	None
At: Vanderbilt University Hospital	Clinical Day	November, once weekly, full time	None
Nashville Academy of Medicine, 647 Doctors Building, Nashville, Tenn.[23] At: Hermitage Hotel	Nashville Medical Assembly	October 28-30, full time	15.00
Southwestern Medical School of the University of Texas, 2211 Oak Lawn Ave., Dallas, Texas [24]	Treatment of Medical Emergencies	September, 3 days, full time	25.00
Postgraduate Medical Assembly of South Texas, 229 Medical Arts Building, Houston, Texas At: The Shamrock Hotel	Medical Assembly	July 20-22, full time	20.00
International Medical Assembly of Southwest Texas, Inc., Box 2445, San Antonio 6, Texas	Graduate Assembly	January 26-28, full time	20.00
Rocky Mountain Medical Conference, 42 South Fifth East St., Salt Lake City, Utah [66]	Medical Conference	July 9-11, full time	None
University of Washington School of Medicine, Seattle 5, Wash.[25]	Drug Therapy	November 19-21, full time	25.00
Washington Academy of General Practice, 426 Medical Center Building, Spokane, Wash. At: Yakima, Wash.	Scientific Assembly	October 30-31, full time	None
Interstate Postgraduate Medical Association, 16 N. Carroll St., Madison 3, Wis.[26] At: Palmer House, Chicago	Annual Refresher Postgraduate Course	November 2-5, full time	5.00
University of Wisconsin Medical School, 418 North Randall Ave., Madison, Wis.	Observation Course in Medicine	Arranged, 1-6 months, full time	100.00 per month
Jackson Clinic, Milwaukee, Wis.[27] At: Methodist Hospital	Jackson Clinic Postgraduate Meeting	October 3, full time	None
NEUROLOGICAL SURGERY			
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	551-A The Intervertebral Disc	October 5-9, full time	60.00
	552-A Diagnosis and Treatment of Peripheral Nerve Injuries	January 11-15, full time	90.00
NEUROLOGY AND PSYCHIATRY			
Los Angeles Psychoanalytic Society, 407 Commercial Center St., Beverly Hills, Calif.	Professional Training in Psychoanalysis [67]	July-January, weekly, arranged	232.00
University of California Medical Extension, 10851 LeConte Ave., Los Angeles 24, Calif. At: Veterans Administration Hospital	Techniques of Hypnosis (Advanced)	Twice weekly, 8 weeks, part time	100.00
Yale University School of Medicine, 333 Cedar St., New Haven, Conn.[28]	Postgraduate Seminar [68]	September 30-December 9, twice weekly, part time	None
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Personal Course in Clinical Neurology	September 23, 10 days, part time	100.00
	Personal Course in Neuropathology	Arranged, part time	20.00 per hour
University of Kansas, Medical Center, 39th St. and Rainbow Blvd., Kansas City, Kan.[29] At: Menninger Foundation, Topeka	Psychosomatic Medicine: Male and Female Reproductive Systems	December 10-12, full time	25.00
Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, La.	Psychosomatic Problems in General Practice	November 16-21, full time	50.00
Massachusetts Department of Mental Health, 15 Ashburton Place, Boston, Mass. At: Metropolitan State Hospital, Waltham, Mass.	Postgraduate Seminar Review Course in Basic Neurology and Psychiatry	October 5-December 7, once weekly, part time	None
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: Jewish Hospital	Child Psychiatry	October, 10 weeks, once weekly, part time	20.00
American Institute for Psychoanalysis, 220 W. 98th St., New York, N. Y.	The Neurotic Patient in Medical Practice	September 15, 10 weeks, once weekly, part time	30.00
	Clinical Conferences for Certified Analysts	September 17, 10 weeks, once weekly, part time	40.00
	Clinical Conference on Case Histories II	September 15, 15 weeks, once weekly, part time	45.00

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NEUROLOGY AND PSYCHIATRY—Continued			
American Institute for Psychoanalysis, 220 W. 98th St., New York, N. Y.	Continuous Case Seminar	September 14, 10 weeks, once weekly, part time	$40.00
	The Psychoanalytic Process	September 15, 15 weeks, once weekly, part time	60.00
	Introduction to Psychoanalytic Technique	September 14, 7 weeks, once weekly, part time	21.00
	Readings in Psychoanalysis. Part I The Works of Karen Herney	November 2, 25 weeks, once weekly, part time	75.00
	Readings in Psychoanalysis. Part II The Works of Freud	September 18, 20 weeks, once weekly, part time	60.00
At: New School for Social Research	Group Psychoanalysis	September 25, 10 weeks, once weekly, part time	14.00
	Neuroses and Psychoses	September 22, 15 weeks, once weekly, part time	21.00
	The Growing Child: A Psychoanalytic Approach	September 21, 15 weeks, once weekly, part time	21.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y.			
At: Mount Sinai Hospital	Neurology PM 31 Neuropathology	October 2-December 4, once weekly, part time	60.00
	Psychiatry PM 31 Techniques of Psychotherapy	October 13, March 2, once weekly, part time	100.00
At: Montefiore Hospital	Neurology PM 61 Advanced Neurology	3 months, continuously, full time	150.00
	Neurology PM 62 Review of Neurology	September 16-December 9, 3 days weekly, part time	150.00
At: Columbia Presbyterian Medical Center	Psychiatry PM 1, Symposium on Neurology and Psychiatry	October 5-December 11, full time	250.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Reading in Psychoanalytic Literature	Fall, 15 weeks, part time	50.00
	Integration of Psychoanalytic Orientations	October, 15 weeks, part time	50.00
	Personality Structures and Psychoanalysis	Fall, 15 weeks, part time	50.00
	Psychiatry and Psychoanalysis	January, 12 weeks, part time	40.00
	Comprehensive Course in Psychiatry	October, 3 years, 5 nights weekly, part time	500.00
	Introductory Lecture in Child Psychiatry	Fall, part time	40.00
New York University, Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	643-A Treatment Methods in Psychiatry	January 11-March 6, part time	250.00
	644-A Neuroanatomy and Neurophysiology	September 14-December 5, 3 days a week, part time	250.00
	645-A Neurology (Graduate Course)	July 1-September 14, full time	700.00
	646-A Psychiatry in the Practice of Medicine and Pediatrics	Arranged, 3 months, full time	300.00
	647-A Psychiatry and Neurology	September 21-December 12, full time	300.00
	648-A Psychology and Psychodynamics	September 14-December 4, part time	Not given
	649-A Psychiatry (Graduate Course)	July 1-September 14, full time	700.00
Postgraduate Center for Psychotherapy, Inc., 218 E. 70th St., New York, N. Y.	Review Courses [69]	Weekly, Fridays, part time	Not given
	Clinical Psychiatry and Diagnosis	15 weeks, once weekly, part time	35.00
	Treatment of Speech Disorders	5 weeks, once weekly, part time	15.00
	Psychopathology and Psychodynamics	15 weeks, once weekly, part time	35.00
	Introduction to Psychotherapy and Psychotherapeutic Techniques	15 weeks, once weekly, part time	35.00
	Clinical Conferences	15 weeks, once weekly, part time	35.00
	Reading in Psychiatry and Allied Fields, Part II	15 weeks, once weekly, part time	35.00
	Dream Interpretation	10 weeks, once weekly, part time	25.00
	The Handling of Special Problems in Therapy	5 weeks, once weekly, part time	25.00
	Continuous Case Seminar	15 weeks, once weekly, part time	35.00
	Symposium for Physicians	5 sessions, once a month, part time	None
Albert Einstein Medical Center, Southern Division, 5th and Reed Sts., Philadelphia 47, Pa.	Psychiatry	Fall, once weekly, part time	None
American College of Physicians, 4200 Pine St., Philadelphia, Pa. At: Jefferson Medical College of Philadelphia	Clinical Neurology [95]	November 2-7, full time	30.00 members 60.00 non-members
University of Pennsylvania, Graduate School of Medicine, Philadelphia 4, Pa.	Clinicobiologic Neurology-Psychiatry [70]	September 28-December 4, full time	300.00
	Neurology-Psychiatry [48]	September 28-May 22, full time	960.00
University of Washington School of Medicine, Seattle 5, Wash.[26]	Practical Psychiatry	July 27-31, full time	50.00
OBSTETRICS AND GYNECOLOGY			
University of California School of Medicine (Medical Extension), Medical Center, San Francisco, Calif. At: University of California, Extension Bldg.	Gynecological and Obstetrical Conference	September 2-4, full time	Not given
University of Colorado, Medical Center, 4200 E. Ninth Ave., Denver, Colo.	Refresher Course	Arranged, 1-2 weeks, full time	35.00
Chicago Medical Society, 86 E. Randolph St., Chicago, Ill. At: Sheraton Hotel	Obstetrics and Gynecology	November 16-20, full time	75.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Twenty-hour Personal Course in Vaginal Approach to Pelvic Surgery	September 14 and November 2, 1 week, full time	100.00
	Intensive Course in Gynecology	September 21 and October 19, 2 weeks, full time	150.00
	Intensive Course in Obstetrics	October 5 and November 2, 2 weeks, full time	150.00
	Personal Course in Gynecologic Surgery	September 9 and November 4, 5 days, part time	100.00
	Personal Course in Office Gynecology	September 9 and November 4, 4 days, part time	100.00
	Personal Course in General and Office Obstetrics	July 1 and October 21, 4 days, part time	100.00
	Personal Course in Surgical Obstetrics	September 2 and November 18, 4 days, part time	100.00

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Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
OBSTETRICS AND GYNECOLOGY—Continued			
Iowa Academy of General Practice, 912 Equitable Bldg., Des Moines, Iowa At: Hotel Savery	Medicine-Obstetrics	September 25, 1 day, full time	Non-members $5.00 members free
State University of Iowa, College of Medicine, Iowa City, Iowa At: University Hospital	Obstetrics and Gynecology	Arranged, 1½ days, full time	10.00 [71]
University of Kansas Medical Center, 39th St. and Rainbow Blvd., Kansas City, Kan.[30]	Gynecology	November 9-11, full time	30.00
Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, La.	Surgery, Gynecology and Traumatology	January 11-16, full time	50.00
Johns Hopkins University School of Medicine, 710 N. Washington St., Baltimore, Md. At: Johns Hopkins Hospital	Gynecological Pathology	October 1, December 1 and February 1, 8 weeks, full time	150.00
Harvard Medical School, Courses for Graduates, 25 Shattuck St., Boston, Mass. At: Free Hospital for Women	Pathology of Obstetrics and Gynecology	January 7-May 13, Thursdays only, part time	155.00
	Gynecology 2	July, August and September, 1 month, full time	155.00
At: Massachusetts General Hospital	Gynecology 3	September 14-25, full time	155.00
At: Boston Lying-In Hospital	Clinical Obstetrics	October-November, 1 month, full time	155.00
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.	Obstetrics for General Physicians	December 2-4, full time	25.00
University of Buffalo School of Medicine, 24 High St., Buffalo, N. Y.	Obstetrics and Office Gynecology	November 18-19, full time	25.00
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: St. John's Episcopal Hospital	Office Gynecology	October, 8 weeks, once weekly, part time	20.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Margaret Hague Maternity Hospital, Jersey City, N. J.	Obstetrics PM 80 Internship Training	3 months, continuously, full time	350.00
	Obstetrics PM 81 Observation Course	1 month, continuously, full time	100.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	General Fertility and Sterility	Arranged, 2 weeks, part time	200.00
	Advanced Course in Fallopian Tube Physiology, Pathology, Diagnosis and Treatment	Arranged, 2 weeks, part time	150.00
	Advanced Course in Culdoscopy in Sterility	Arranged, 2 weeks part time	150.00
	Advanced Course in Endometrial Biopsy and Ovulitation	Arranged, part time	150.00
	Advanced Course in Operative (Reparative and Restorative) Gynecology in Sterility	Arranged, 2 weeks, part time	150.00
	Advanced Course in Semen and Semen Analysis	Arranged, 1 week, part time	75.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Clinical Gynecology	Arranged, 6 weeks, part time	75.00
	Clinical and Operative (Cadaver) Gynecology	Arranged, 6 weeks, part time	175.00
	Obstetrics and Gynecology [72]	October, 2 months, full time	250.00
	Manikin Obstetrics	Arranged, 4 weeks, part time	100.00
	Clinical Course in Office and General Obstetrics	Arranged, 4 weeks, part time	100.00
	Culdoscopy	Arranged, twice weekly, part time	100.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	560-A Diagnosis and Therapy of Malignant Neoplasms of the Female Genital Tract	September 14-June 17, twice weekly, part time	300.00
	561-A Seminar in Gynecology	October 5-31, full time	150.00
	562-A Technique of Gynecological Examination	October 26-November 16, 3 days a week, part time	50.00
	564-A Infertility	December 7-9, full time	40.00
	565-A Electrical Medalities in Gynecology (for Specialists)	October 12-November 13, twice weekly, part time	75.00
	566-A Culdoscopy	November 30-December 4, 3 days a week, part time	50.00
	567-A Gynecological Endocrinology	October 6-December 3, 3 days a week, part time	125.00
	568-A Gynecological Cytology (for Specialists)	October 6-December 3, twice weekly, part time	100.00
	569-A Surgical Anatomy as Applied to Gynecology	September 8-October 9, 3 days a week, part time	175.00
	5610-A X-ray Diagnosis in Obstetrics and Gynecology	Arranged, 3 days, part time	45.00
	734-A Gynecology (for Specialists)	September 8-December 24, part time	250.00
Southern Pediatric Seminar, Saluda, N. C.	Obstetrical Course	August 3-8, full time	25.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Gynecology-Obstetrics [48]	September 28-May 22	900.00
Tennessee State Medical Association, Postgraduate Committee, 4 S. Dunlap St., Memphis, Tenn. At: 45 Teaching centers or county seat towns	Obstetrics	September 1, 1953-September 1, 1955, 10 weeks in each circuit, once weekly, part time	20.00
Southwestern Medical School of the University of Texas, 2211 Oak Lawn Ave., Dallas, Texas [24]	Psychosomatic Medicine	December, 3 days, full time	25.00
University of Puerto Rico School of Medicine, San Juan, P. R.[31]	Cytology and Cytologic Technique in Gynecology	Arranged, 16 hours, part time	None
OPHTHALMOLOGY AND OTOLARYNGOLOGY			
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Basic Science in Otolaryngology [55]	September 28-June 4, full time	800.00
University of California School of Medicine (Medical Extension), Medical Center, San Francisco, Calif.[32] At: University of California Hospital	Ophthalmology (for Specialists)	September 7-12, full time	Not given
	Ophthalmology (for Specialists)	September 15-20, full time	75.00

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Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
OPHTHALMOLOGY AND OTOLARYNGOLOGY—Continued			
At: University of California, Medical Center, San Francisco	Resident Course in Ophthalmology	Between September and January, part time	$200.00
University of Colorado, Medical Center, 4200 E. Ninth Ave., Denver, Colo.[33]	Postgraduate Seminar	August 3-6, full time	40.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Two-Week Clinical Course in Ophthalmology	1st of every week, full time	50.00
	Two-Week Clinical Course in Otolaryngology	1st of every week, full time	50.00
Illinois Masonic Hospital, 836 Wellington Ave., Chicago, Ill.	Surgery of Septum and External Nasal Pyramid	October, 8 days, full time	200.00
Northwestern University Medical School, 303 East Chicago Ave., Chicago, Ill.	Basic Science Course in Extraocular Muscles [48]	September 14-26, part time	100.00
	Basic Science Course in Extraocular Muscles [48]	Arranged, 3 days, full time	150.00
	Postgraduate Basic Course in Ophthalmology	January 4-June 18, full time	500.00
	Endaural Otologic Surgery and Audiology	September 14-October 10, full time [73]	500.00
University of Illinois College of Medicine, 1853 W. Polk St., Chicago 12, Ill.	Annual Otolaryngological Assembly	September 21-October 3, full time	175.00 [74]
	Basic Otolaryngology [55]	October 1-June 30, full time	750.00
At: Illinois Eye and Ear Infirmary	Postgraduate Course in Ophthalmology	July 1-December 31, full time	500.00
State University of Iowa College of Medicine, Iowa City, Iowa			
At: University Hospital	Ophthalmology Conference	Monthly, first Wednesday, full time [75]	None
Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, La.	Basic Science Course in Ophthalmology	July 6-June 30, full time	500.00
	Ophthalmic Pathology	November 30-December 5, full time	100.00
University of Maryland School of Medicine, 29 S. Greene St., Baltimore, Md.	Anatomy of the Head and Neck as Applied to Eye, Ear, Nose and Throat Surgery [76]	Arranged, October, twice weekly, part time	150.00
Harvard Medical School, Courses for Graduates, 25 Shattuck St., Boston 15, Mass.			
At: Harvard Medical School and Massachusetts Eye and Ear Infirmary	Basic Science Course in Ophthalmology [77]	September 28-February 27, full time	705.00
	Basic Sciences in Otolaryngology	November 2-March 27, full time	930.00
At: Massachusetts Eye and Ear Infirmary	Basic Sciences in Ophthalmology	September-December, 3 weeks, full time	400.00
Tufts College Medical School, Postgraduate Division, 30 Bennet St., Boston, Mass.			
At: Boston City Hospital	Neuro-Ophthalmology	November 16-20, full time	80.00
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich.	Basic Ophthalmology	September 14-June, 9 months, full time	900.00
American Academy of Ophthalmology and Otolaryngology, 100 First Ave. Bldg., Rochester, Minn.	Home Study Course in Ophthalmology	September 1-June 30, part time	20.00
	Home Study Course in Otolaryngology	September 1-June 30, part time	20.00
At: Palmer House, Chicago	Instruction Courses, Ophthalmology, Otolaryngology and Maxillofacial Surgery	October 11-16, part time	2.00 per hour
Washington University School of Medicine, 640 S. Kingshighway, St. Louis 10, Mo.	Basic Course in Ophthalmology [48]	September-May, full time	800.00
American Academy of Plastic Surgery for Head and Neck, 307 Second Ave., New York, N. Y.			
At: Manhattan General Hospital	Otolaryngologic Plastic Surgery	September 16-October 8, full time	250.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y.			
At: Mount Sinai Hospital	Otorhinology PM 30 Rhinoplasty and Otoplasty	September 16-December 16, once weekly, part time	250.00
At: Montefiore Hospital	Ophthalmology PM 60 Elementary Ophthalmoscopy	January 4-March 1, once weekly, part time	30.00
	Ophthalmology PM 62 Glaucoma	October 19-December 7, once weekly, part time	30.00
New York Eye and Ear Infirmary, 218 2nd Ave., New York, N. Y.	Physiological Optics in Clinical Practice	Arranged, 6 weeks, part time	100.00
	Plastic Eye Surgery	Arranged, 4 weeks, part time	150.00
	Anomalies of Extraocular Muscles	Arranged, 4 weeks, part time	75.00
	Slit Lamp Microscopy	Arranged, 4 weeks, part time	100.00
	Ophthalmoscopy	Arranged, 4 weks, part time	75.00
	Glaucoma	Arranged, 8 weeks, part time	75.00
	Refraction	Arranged, 8 weeks, part time	100.00
	Perimetry	Arranged, 4 weeks, part time	75.00
	Neuro-Ophthalmology	Arranged, 4 weeks, part time	75.00
	Roentgenology	Arranged, 1 week, part time	50.00 for eye 50.00 for ear
	Resuscitation	Arranged, 1 week, part time	50.00
	The Conservative Management of Acute Sinusitis and Chronic Rhinitis	Arranged, 6 hours, part time	75.00
	Rehabilitation of the Hard of Hearing	Arranged, 4 hours, part time	75.00
	Clinical Histopathology of the Eye	Arranged, 16 hours, part time	75.00
	Broncho-Esophagology and Laryngeal Surgery	Arranged, 12 days, part time	250.00
	External Disease of the Eye	Arranged, 5 days, part time	75.00
	Clinical Physiopathology of the Ear	Arranged, 10 hours, part time	150.00
	Didactic and Operative Work in Rhinoplasty and Otoplasty	Arranged, 4 weeks, part time	250.00
	Allergy (Eye and Ear)	Arranged, 36 days, part time	150.00 for eye 150.00 for ear
At: New York University College of Medicine	Operative Eye Surgery	Arranged, 4 weeks, part time	150.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Otolaryngology and Ophthalmology	October 1, 9 months, full time	1,000.00
	Otolaryngology and Ophthalmology [78]	October and January, 3 months, full time	600.00

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Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
OPHTHALMOLOGY AND OTOLARYNGOLOGY—Continued			
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Surgical Anatomy of Nose and Accessory Sinuses	Arranged, 4 weeks, part time	$150.00
	Clinical Ophthalmology	Arranged, 6 weeks, full time	75.00
	Clinical Ophthalmology	Arranged, 3 months, full time	100.00
	Clinical Otolaryngology	Arranged, 6 weeks, part time	100.00
	Clinical Otolaryngology	Arranged, 3 months, full time	150.00
	Clinical Ophthalmology and Otolaryngology	Arranged, 6 weeks, part time	150.00
	Clinical Ophthalmology and Otolaryngology	Arranged, 3 months, part time	250.00
	Operative Nose and Throat (Dissection)	Arranged, 4 weeks, part time	150.00
	Operative Otology (Cadaver)	Arranged, 4 weeks, part time	100.00
	Head and Neck Dissection	Arranged, 4 weeks, part time	150.00
	Seminar in Ophthalmology and Otolaryngology	Arranged, 5 days, full time	50.00
	Operative Ophthalmology (Dissection)	Arranged, 4 weeks, part time	100.00
	Motor Anomalies	Arranged, 4 weeks, part time	50.00
	Ophthalmology [79]	Arranged, 3 months, part time	300.00
	Refraction	Arranged, 4 weeks, part time	100.00
	Advanced Otology	Arranged, 2 weeks, part time	250.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	574-A Surgery of the Eye (for Specialists)	October 26-31, full time	100.00
	575-A Differential Diagnosis with the Slit Lamp (for Specialists)	November 2-6, part time	75.00
	576-A Ophthalmology	September 28-June 18, full time	700.00
	577-A External Diseases of the Eye (for Specialists)	November 2-6, part time	Not given
	578-A Ocular Expressions of Systemic Diseases	September 14-18, part time	50.00
	591-A Intensive Course in Basic Sciences (Otorhinolaryngology)	September 14-25, part time	100.00
	592-A Histopathology of the Ear, Nose and Throat	September 14-25, part time	100.00
	593-A Basic Sciences of Otorhinolaryngology	September 28-June 18, full time	700.00
	594-A Endaural Surgery	November 9-20, full time	200.00
	596-A Anatomy of the Head, Neck and Throat (for Otolaryngologists)	September 28-November 6, part time	125.00
	597-A Neuroanatomy, Neurophysiology and Neuro-Otology	November 2-6, full time	75.00
	598-A Pathology of the Head and Neck	November 9-December 18, part time	125.00
	599-A Rhinology, Sinus and Nasal Surgery	December 7-11, full time	100.00
	5711-A Ophthalmoscopy	September 15-October 8, twice weekly, part time	50.00
	5713-A Ocular Therapeutics	October 27-November 19, twice weekly, part time	50.00
	5714-A Histopathology	September 14-19, part time	100.00
	5910-A Laryngology and Surgery of the Larynx and Neck	January 4-15, full time	200.00
	5911-A Advanced Surgery of the Neck	Arranged, 10 days, full time	250.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Ophthalmology [48]	September 28-May 22, full time	960.00
	Otolaryngology [48]	September 28-May 22, full time	960.00
Virginia Society of Otolaryngology and Ophthalmology, 1200 E. Broad St., Richmond 19, Va. At: Medical College of Virginia	Clinical Session—Postgraduate	November 30-December 3, full time	35.00 [80]
ORTHOPEDIC SURGERY			
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles, Calif.	Diseases and Injuries of Bones and Joints	July 6-31, full time	100.00
Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, La.	Basic Science as Applied to Orthopedics [81]	September 1, 5 months, full time	300.00
Harvard Medical School, Courses for Graduates, 25 Shattuck St., Boston, Mass. At: Massachusetts General Hospital	Treatment of Fractures and Other Traumatic Conditions	September 28-October 3, full time	155.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Fractures and Allied Trauma	Fall, 4 weeks, full time	200.00
	Orthopedics in General Practice	November, 1 week, full time	60.00
	Orthopedics of the Foot	Arranged, 8 weeks, part time	100.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Orthopedic Surgery for General Surgeons	Arranged, 3 months, part time	75.00
	Operative Orthopedics (Dissection)	Arranged, 5 days, part time	100.00
	Advanced Orthopedics of the Foot	Arranged, 8 days, part time	100.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	581-A Basic Science as Related to Orthopedic Surgery	January 4-June 18, full time	450.00
	583-A Anatomy for Orthopedic Surgeons	January 4-8, full time	90.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Orthopedics [48]	September 28-May 22, full time	960.00
PATHOLOGY			
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	General and Surgical Pathology	September 29-June 3, twice weekly, part time	175.00
Armed Forces Institute of Pathology, 7th and Independence Avenue, S. W., Washington 25, D. C.	Forensic Pathology [49,50,51,52]	November 2-6, 10 sessions, part time	None
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Course in Gross and Surgical Pathology	Arranged, 1 year, full time	900.00
	Course in Gross and Microscopic Pathology	Arranged, 1 year, full time	500.00
	Personal Course in Surgical Pathology	Arranged, 2-4 or more weeks, full time	150.00 2 weeks
	Personal Course in Surgical Pathology on Selective Subjects	Arranged, 1-2 weeks, full time	15.00 per hour
	Clinical Course in Gross and Surgical Pathology	Arranged, 6 months, full time	500.00
University of Maryland School of Medicine, 29 S. Greene St., Baltimore, Md.	Neuropathology [82]	Arranged, 6 months, full time	210.00

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Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	PATHOLOGY—Continued		
University of Michigan Medical School, Ann Arbor, Mich.	Basic Sciences (Pathology)	September 21-December 4, 11 weeks, full time	$250.00
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich.	Neuropathology	December 7-March 13, 12 weeks, once weekly, part time	50.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y.			
At: Columbia Presbyterian Medical Center	Pathology PM 1 Surgical Pathology	July 1, 6 months, full time	230.00
	Pathology PM 1 Surgical Pathology	July 1, 12 months, full time	460.00
At: Mount Sinai Hospital	Pathology PM 30 General and Special Pathology	October 3-January 9, once weekly, part time	60.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Pathology	Arranged, 16 weeks, part time	200.00
	Clinical Pathology	Arranged, 26 hours, part time	100.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Pathology	Arranged, 3 months, part time	$300.00
	Pathology	Arranged, 12 months, part time	1,000.00
	Pathology for Surgeons	Arranged, 1 month, part time	100.00
	Surgical Pathology	Arranged, 3 months, part time	300.00
	Urological Pathology	Arranged, 3 months, part time	50.00
	Gynecological Pathology	Arranged, 2 weeks, part time	200.00
	Blood Transfusions	Arranged, 2 weeks, part time	100.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	442-A Surgical Pathology (for Specialists)	September 22-January 7, twice weekly, part time	200.00
	443-A Principles of Pathology	September 28-December 16, twice weekly, part time	100.00
	444-A Special Pathology for Surgeons	January 7-June 17, once weekly, part time	125.00
Hillcrest Medical Center, Twelfth St. and Utica Ave., Tulsa, Okla.	Clinical Pathological Conference	Arranged, once every two weeks, part time	None
	PEDIATRICS		
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Department Course in Pediatrics [83]	July 1, 1 year, full time	750.00
	Clinical Refresher Course in Pediatrics	Arranged, 2 weeks, full time	60.00
		Arranged, 1 month, full time	100.00
	Personal Course in Pediatrics	September 23, 10 days, part time	100.00
	The Diagnosis and Treatment of Congenital and Rheumatic Heart Disease in Infants and Children	September 23, 10 days, part time	100.00
Louisiana State Department of Health, 418 Royal St., New Orleans, La.			
At: Various sections throughout the State	Circuit Course	4 successive evenings, twice annually	None
At: Louisiana State University School of Medicine	Pediatric Refresher Course	Arranged, October, 3 days, full time	Not given
Harvard Medical School, Courses for Graduates, 25 Shattuck St., Boston, Mass.			
At: Massachusetts General Hospital	Pediatrics 1	October 1-May 31, full time	$605.00
At: Children's Hospital	Pediatrics 2	September 1-December 18 and January 4-April 23, full time	505.00
Tufts College Medical School, Postgraduate Division, 30 Bennet St., Boston, Mass.			
At: Boston Floating Hospital and Boston Dispensary	Pediatrics I	November 2-6, full time	45.00
At: Boston Floating Hospital	Pediatrics II	November 2-13, part time	30.00
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.	Pediatrics for General Physicians	January 7-9, full time	25.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Clinical Pediatrics	Arranged, 1 month, full time	150.00
	Clinical Pediatrics	Arranged, 3 months, full time	250.00
	Clinical Pediatrics	Arranged, 6 months, full time	450.00
	Clinical Pediatrics	Arranged, 9 months, full time	650.00
	Clinical Pediatrics	Arranged, 1 year, full time	850.00
	Pediatric Allergy Course I	October, 20 weeks, once weekly part time	300.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Pediatrics	Arranged, 4 weeks, part time	75.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	6110-A Pediatrics	September 14, 9 months, full time	700.00
	611-A Clinical Pediatrics	November 2-January 13, 3 days weekly, part time	125.00
	612-A Clinical Pediatrics	October 5-30, full time	150.00
	614-A Review of Clinical Pediatrics	September 21-26, full time	50.00
	617-A Communicable Diseases	January 11-15, full time	50.00
	618-A Pediatric Cardiology	September 14-18, full time	50.00
Southern Pediatric Seminar, Saluda, N. C.	Pediatric Course	July 20-August 1, full time	40.00
Frank E. Bunts Educational Institute, 2020 E. 93rd St., Cleveland 6, Ohio	Current Therapy in Pediatrics	October 7-8, full time	15.00
Hillcrest Medical Center, Twelfth St. and Utica Ave., Tulsa, Okla.	Pediatrics (Postgraduate and Continuation)	Arranged, once weekly, part time	None
St. Christopher's Hospital for Children, 2600 N. Lawrence St., Philadelphia, Pa.[84]	Postgraduate Course in Pediatrics for the General Practitioner	November-March, 20 weeks, once weekly, part time	50.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Pediatrics [48]	September 28-May 22, full time	960.00
At: Children's Hospital	Practical Pediatric Hematology	September 15-17, full time	60.00
Asociacion Medica de Puerto Rico, San Juan, P. R.[85]			
At: In districts of Puerto Rico	Refresher Course in Pediatrics	July-December, once weekly, part time	None
	PHARMACOLOGY		
State University of Iowa College of Medicine, Iowa City, Iowa	Advanced Pharmacology	Arranged, 1 hour weekly, part time	None
	PHYSICAL MEDICINE AND REHABILITATION		
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Physical Medicine	September 30-November 18, once weekly, part time	30.00
University of Southern California, Division of Graduate Medicine, 1200 N. State St., Los Angeles, Calif.			
At: Los Angeles County Hospital	‡879 Advanced Clinical Practice in Physical Medicine	1 year, arranged, full time	1,000.00

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Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
PHYSICAL MEDICINE AND REHABILITATION—Continued			
American Congress of Physical Medicine and Rehabilitation, 30 N. Michigan Ave., Chicago 2, Ill. At: Palmer House	Instruction Seminar	Every day, August 31-September 4, part time	[84]
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.	Rehabilitation for General Physicians	October 22-24, full time	$25.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Columbia Presbyterian Medical Center	Physical Medicine and Rehabilitation PM I	July 1, 6 months, full time	230.00
	Physical Medicine and Rehabilitation PM	July 1, 12 months, full time	460.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Physical Medicine and Rehabilitation	Arranged, 4 weeks, full time	100.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.[86]	738-A Physical Medicine and Rehabilitation (Graduate Course)	September 28-June 18, full time	700.00
	738-B Physical Medicine and Rehabilitation (Graduate Course)	January 11-October 8, full time	700.00
	739 Physical Medicine and Rehabilitation	Arranged, 12 weeks	200.00
	739 Physical Medicine and Rehabilitation	Arranged, 24 weeks	400.00
	7310-A Physical Medicine and Rehabilitation	September 21-October 16, full time	100.00
	7310-A Physical Medicine and Rehabilitation	January 11-February 5, full time	100.00
	7312-A Seminar on the Rehabilitation of Children	October 19-23, full time	40.00
	7312-A Seminar on the Rehabilitation of Children	January 18-22, full time	40.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Physical Medicine [48]	September 28-May 22, full time	960.00
PHYSIOLOGICAL CHEMISTRY			
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Biochemical Background of Clinical Medicine	September 23, 10 days, part time	125.00
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich.	Seminar	September 14-December 5, December 7-March 13, 12 weeks, once weekly, part time	15.00
	Special Topics	September 14-December 5, 12 weeks, once weekly, part time	15.00
PHYSIOLOGY			
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Surgical Physiology	October 1-June 3, once weekly, part time	75.00
Mercy Hospital, San Diego, Calif.	Formal Basic Science and Continuation Course in Applied Physiology	October-August, weekly, part time	None
San Diego County General and Mercy Hospitals, San Diego, Calif.	Formal Basic Science Course	October-August, alternate weeks, part time	[85]
Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington 12, D. C.	Symposium on Circulation and Hemostasis [49,50,51,52]	October 5-9, full time	None
State University of Iowa College of Medicine, Iowa City, Iowa	Advanced Physiology	September-February, once weekly, part time	None
	Physiology of Aging	September-February, once weekly, part time	None
Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, La.	Applied Physiology	Annually, Monday evenings, part time	50.00 per semester
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Mount Sinai Hospital	Physiology PM 32 Normal and Pathological Physiology	October 21-April 7, once weekly, part time	100.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Physiology of the Cardio-Vascular System and Blood	Arranged, 1 month, part time	75.00
	Physiology and Respiration	Arranged, 1 month, part time	75.00
	Physiology of the Nervous System	Arranged, 2 weeks, part time	50.00
	Physiology of the Special Senses	Arranged, 1 month, part time	75.00
	Physiology of the Endocrine System	Arranged, 1 month, part time	75.00
	Physiology and Chemistry of the Gastrointestinal Tract, Digestion	Arranged, 1 month, part time	150.00
	Applied Physiology	Arranged, 36 days, part time	300.00
	Histology	Arranged, 5 weeks, full time	300.00
	Newer Concepts in the Physiology of Cancer	Arranged, 6 weeks, part time	150.00
	Nutrition	Arranged, 1 month, part time	150.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	5420-A Normal and Pathological Physiology: Functional and Chemical Aspects	September 21-October 2, full time	100.00
POLIOMYELITIS			
Orthopaedic Hospital, 2400 S. Flower St., Los Angeles, Calif.[87]	Poliomyelitis	October 26-30, full time	15.00
Georgia Warm Springs Foundation, Warm Springs, Ga.[87]	Care of Poliomyelitis	October and January, 1 week, full time	None
The Children's Medical Center, 300 Longwood Ave., Boston, Mass.[87]	Refresher Course	August 3-7, full time	50.00
University of Pittsburgh School of Medicine, 3941 O'Hara St., Pittsburgh 13, Pa. At: D. T. Watson School of Physiatrics, Leetsdale	Management of Acute Poliomyelitis with Emphasis on Prescription of the Respirator and Rocking Bed	Arranged, 5 days minimum, full time	10.00 [88]
PROCTOLOGY			
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago 12, Ill.	Lectures and Cadaver Course in Proctology	October 14, 5 days, part time	100.00

References will be found on page 647.

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Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	PROCTOLOGY—Continued		
Tufts College Medical School, Postgraduate Division, 30 Bennet St., Boston, Mass. At: Boston Dispensary and Mount Auburn Hospital	Proctology I	October 19-23, full time	$45.00
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1] At: Jewish Hospital	Proctology	October, 6 weeks, twice weekly, part time	40.00
	PUBLIC HEALTH		
University of California School of Public Health, Berkeley, Calif.	Graduate Study [87]	September-June, full time	194.00 [88]
Johns Hopkins University School of Hygiene and Public Health, 615 N. Wolfe St., Baltimore, Md.	Master of Public Health	September-June, full time	800.00
	Doctor of Public Health [89]	September-May, full time	800.00
Harvard University School of Public Health, 55 Shattuck St., Boston, Mass.	Public Health	September 28-June 17, full time	800.00
Albany Medical College, 47 New Scotland Ave., Albany 3, N. Y At: Albany, Syracuse, Rochester, Buffalo, Poughkeepsie	Extension Course in Public Health	Arranged, 6 days, part time	25.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: School of Public Health	Occupational Medicine 201 Introduction to Occupational Medicine	November 23-January 30, once weekly, part time	25.00
Columbia University School of Public Health, 600 W. 168th St., New York 32, N. Y.	Hospital Administration	September 24, 21 months, full time	1,045.00
	Public Health	September 24, 9 months, full time	835.00
	Administrative Medicine	September 24, 21 months, full time	1,045.00
University of Pittsburgh, Graduate School of Public Health, Pittsburgh 13, Pa.	Public Health Practice, Occupational Health, and Hospital Administration	September-June, full time	700.00
	PULMONARY DISEASES		
Department of the Army, Office of the Surgeon General, Washington 25, D. C. At: Fitzsimons Army Hospital, Denver, Colo.	Symposium on Pulmonary Diseases [49,50,51,52]	September 21-25, full time	None
Public Health Service, Communicable Disease Center, Atlanta, Ga.	Laboratory Diagnosis of Tuberculosis	November 9-13, full time	None
	Laboratory Diagnosis of Tuberculosis	November 16-27, full time	None
	Laboratory Methods in the Study of Pulmonary Mycoses	November 30-December 11, full time	None
American College of Chest Physicians, 112 E. Chestnut St., Chicago, Ill. At: Hotel New Yorker, New York City	Postgraduate Course in Diseases of the Chest	November 2-6, full time	75.00
At: Knickerbocker Hotel, Chicago	Postgraduate Course in Diseases of the Chest	September 28-October 2, full time	75.00
University of Minnesota, Center for Continuation Study, Minneapolis, Minn.[38]	Diseases of Chest for General Physicians	October 15-17, full time	25.00
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Montefiore Hospital	Medicine PM 71 Diseases of the Chest	January 8-May 29, once weekly, part time	100.00
At: Bellevue Hospital	Medicine PM 80 Diseases of the Chest	October 1-31, full time	75.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Pulmonary Tuberculosis	Arranged, 3 weeks, full time	175.00
	Diseases of the Chest	October, 2 months, part time	100.00
Saranac Lake Medical Society, P. O. Box 707, Saranac Lake, N. Y.[39]	Tuberculosis Symposium for General Practitioners	July 13-17, full time	40.00 members 50.00 non-members
Ohio State University College of Medicine, Neil and Eleventh Aves., Columbus, Ohio [40]	Course in Pulmonary Diseases	September 25-26, full time	Not given
Southwestern Medical School of the University of Texas, 2211 Oak Lawn, Dallas, Texas [25]	Tuberculosis	October, 3 days, full time	25.00
	RADIOLOGY		
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Roentgenology	September 29-June 1, once weekly, part time	100.00
University of Southern California, Division of Graduate Medicine, 1200 N. State St., Los Angeles, Calif. At: Los Angeles County Hospital	#858 Diagnostic and Therapeutic Radiology	3 months, arranged, full time	250.00
	#858 Diagnostic and Therapeutic Radiology	6 months, arranged, full time	500.00
	#858 Diagnostic and Therapeutic Radiology	9 months, arranged, full time	750.00
	#858 Diagnostic and Therapeutic Radiology	1 year, arranged, full time	1,000.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Course in Diagnostic Radiology and X-Ray Therapy	Arranged, 1 year, full time	750.00
	Course in Diagnostic Roentgenology	Arranged, 8 months, full time	500.00
	Routine Clinical Course in Diagnostic Roentgenology and Fluoroscopy	Arranged, 2 weeks, full time	70.00
	Diagnostic Roentgenology	September 23, 10 days, part time	100.00
	Clinical and Didactic Course in Diagnostic Roentgenology and Fluoroscopy	October and January, 2 weeks, full time	125.00
	High and Low Voltage X-Ray Therapy	Arranged, 1 week, full time	60.00
		Arranged, 2 weeks, full time	110.00
		Arranged, 1 month, full time	200.00
Northwestern University Medical School, 303 E. Chicago, Chicago, Ill.	Radiation Physics [48]	January-May, part time	10.00 residents 25.00 others
University of Kansas Medical Center, 39th St. and Rainbow Blvd., Kansas City, Kan. At: Stormont-Vail Hospital, Topeka	Radioactive Isotopes	September	Not given
University of Minnesota Center for Continuation Study, Minneapolis, Minn.	Radiation Therapy for Radiologists	October 26-31, full time	40.00

References will be found on page 647.

Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	RADIOLOGY—Continued		
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y.			
At: Mount Sinai Hospital	Radiology PM 30 Introduction to Nuclear Radiation Physics	October 14-January 27, twice weekly, part time	$80.00
	Radiology PM 31 Radiology of the Chest	October 19-27, part time	25.00
	Radiology PM 35 Use of Radioactive Iodine	3 months, continuously, part time	250.00
At: Columbia Presbyterian Medical Center	Radiology PM 1 Radiological Physics	January 12-April 2, twice weekly, part time	25.00
	Radiology PM 80 Roentgenographic Interpretation of Diseases of Bones and Joints	October 7-December 23, once weekly, part time	150.00
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1]			
At: Jewish Hospital	X-Ray Diagnosis	October, 10 weeks, once weekly, part time	20.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Diagnostic Roentgenology	Arranged, 6 weeks, part time	150.00
	Radium and Roentgen Therapy	Arranged, 6 weeks, part time	150.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Roentgen Interpretation and Technic	October and January, 3 months full time	300.00
	Advanced Diagnostic Roentgen and Radiotherapy	October and January, 3 months full time	300.00
	Diagnostic Roentgen and Radiation Therapy	October and January, 12 months, full time	1,000.00
	Practical Course in Superficial and Deep X-Ray Therapy	Arranged, 4 weeks, part time	100.00
	Advanced Course in Radiotherapy	Arranged, 4 weeks, part time	100.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	651-A Diagnostic Radiology for General Practitioners	September 30-May 5, once weekly, part time	100.00
	651-B Diagnostic Radiology for General Practitioners	October 2-May 7, once weekly, part time	100.00
	653-A Radiology, Basic Science	September 28-June 18, full time	700.00
	655-A Radiophysics	October 20-February 2, once weekly part time	75.00
Hillcrest Medical Center, Twelfth St. and Utica Ave., Tulsa, Okla.	X-Ray (Conference of Patients in Hospital)	Arranged, once weekly, part time	Not given
American Roentgen Ray Society, Germantown Hospital, Philadelphia 44, Pa.			
At: Netherlands-Plaza Hotel, Cincinnati, Ohio	Instructional Courses	September 29-October 2, 1-4 days, part time	[90]
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Radiology [48]	Septmber 28-May 22, full time	960.00
Institute of Nuclear Studies, Oak Ridge, Tenn.[41]	Advanced Medical Course (Radioisotopes in Medicine)	August 31-September 11, full time	25.00
	Radioisotope Techniques Course (Techniques in Research)	July and August, 4 weeks, full time	25.00
	SURGERY		
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.	Basic Science in Surgery and Surgical Specialties [55]	September 28-June 4, full time	800.00
	Traumatic Surgery	September 29-December 9, twice weekly, part time	50.00
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Course in Surgical Technic, Clinical Surgery, Surgical Anatomy, Pre- and Post-Operative Management	August 3 and October 26, 4 weeks, full time	325.00
	Personal Course in General Surgery	October 12, 2 weeks, full time	250.00
	Intensive Course in Surgical Technic	2 weeks, full time [91]	250.00
	Course in Surgery of Colon and Rectum	September 21, October 26 and November 30, 1 week, full time	125.00
	Course in Surgical Anatomy of the Cadaver, Clinical Surgery, Pre- and Post-Operative Management	August 17 and November 9, 2 weeks, full time	150.00
	Personal Course in Breast and Thyroid Surgery	October 26, 1 week, full time	150.00
	Personal Course in Gallbladder Surgery	October 26, 3 days, full time	100.00
	Intensive Review Course Considering Basic Principles in General Surgery	September 21, 2 weeks, full time	200.00
	Personal Course in Esophageal Surgery	October 19, 1 week, full time	150.00
	Personal Course in Thoracic Surgery	October 12, 1 week, full tifne	125.00
	Course in the Treatment of Varicose Veins	Arranged, monthly, 2 days, full time	50.00
	Personal Course in General Surgery	October 5, 1 week, full time	150.00
	Course in the Treatment of Varicose Veins	Arranged, monthly, 2 days, part time	50.00
	Personal Course in Clinical Surgery	September 23, 10 days, part time	150.00
	Personal Course in Surgical Diagnosis, Pre- and Post-Operative Management	September 23, 10 days, part time	100.00
	Personal Course in Thoracic Surgery	September 23, 10 days, part time	100.00
	Practical and Didactic Course in Proctoscopy and Sigmodoscopy	September 22 and November 24, 3 days, part time	50.00
	Surgical Anatomy of the Cadaver	September 24, 10 days, part time	125.00
	Surgical Technic with Practice	September 23, 10 days, part time	250.00
Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, La.	Surgery, Gynecology and Traumatology	January 11-16, full time	50.00
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich.	Surgery Seminar	September 14-December 5, December 7-March 13, once weekly, part time	15.00
Joint Committee on Post-Graduate Education, 1313 Bedford Ave., Brooklyn 16, N. Y.[1]			
At: St. John's Episcopal Hospital	Office Surgery	October, 8 weeks, once weekly, part time	20.00
At: Wyckoff Heights Hospital	Practical Aspects of Gastrointestinal Surgery	October, 10 weeks, once weekly, part time	100.00

References will be found on page 647.

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Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
	SURGERY—Continued		
Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York 32, N. Y. At: Mount Sinai Hospital	Surgery PM 30 Surgery of the Gastrointestinal Tract	October 13-November 7, full time	$150.00
At: Columbia Presbyterian Medical Center	Surgery PM 1 Clinical Surgery	July 1, 6 months, full time	230.00
	Surgery PM 1 Clinical Surgery	July 1, 12 months, full time	460.00
	Surgery PM 1-A Surgery	July 1, 6 months, full time	230.00
	Surgery PM 1-A Surgery	July 1, 12 months, full time	460.00
	Surgery PM 2-A Studies in Cardiovascular Surgery	January 1, 6 months, full time	230.00
	Surgery PM 2-A Studies in Cardiovascular Surgery	January 1, 12 months, full time	460.00
	Surgery PM 2 Principles of Cardiovascular Surgery	January 1, 6 months, full time	230.00
	Surgery PM 2 Principles of Cardiovascular Surgery	January 1, 12 months, full time	460.00
Manhattan General Hospital, 307 Second Ave., New York, N. Y.	Rhinoplasty and Otoplasty	September, 2 weeks, full time	250.00
New York Medical College, Flower and Fifth Ave. Hospitals, 1 E. 105th St., New York 29, N. Y.	Surgical Technique	Arranged, 50 days, part time	375.00
	Thoracic Surgery	Full, 3 weeks, part time	375.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Surgical Anatomy	Arranged, 2 weeks, part time	150.00
	Combined Surgical Course [92]	October and January, 3 months, full time	350.00
	Clinical Surgery	October and January, 6 weeks, full time	100.00
	Clinical and Operative (Cadaver) Surgery	October and January, 6 weeks, full time	200.00
	Traumatic Surgery [93]	Arranged, 2 months, part time	200.00
	Thoracic Surgery	Arranged	200.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	665-A Surgery (Graduate Course)	September 28-June 18, full time	700.00
	661-A Review of General Surgery (for Specialists)	October 12-November 7, full time	300.00
	663-A Recent Advances in Surgery	September 21-October 3, full time	200.00
	664-A Trauma (Excluding Fractures)	November 30-December 5, full time	125.00
	666-A Diagnosis and Treatment of Trauma	December 7-12, full time	90.00
	6610-A Trauma of the Genitourinary System	September 8-October 13, once weekly, part time	50.00
Frank E. Bunts Educational Institute, 2020 E. 93rd St., Cleveland, Ohio	Current Problems in General Surgery	October 28-29, full time	15.00
Hillcrest Medical Center, Twelfth St. and Utica Ave., Tulsa, Okla.	General Surgery (Postgraduate Course) [94]	Arranged, once weekly, part time	None
University of Oregon Medical School, 3181 S. W. Sam Jackson Park Rd., Portland 1, Ore.	General Surgery	October 26-30, 5 days	50.00
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	General Surgery [48]	September 28-May 22, full time	960.00
	Advances in Medicine and Surgery	September 21-25, full time	[64]
University of Tennessee College of Medicine, 847 Union Ave., Memphis, Tenn. At: John Gaston Hospital	Primary Trauma	July 15-17, full time	50.00
University of Wisconsin Medical School, 418 N. Randall Ave., Madison, Wis.	Observation Course in Surgery	Arranged, 1-6 months, full time	100.00 per month
American College of Physicians, 4200 Pine St., Philadelphia, Pa. At: University of Utah College of Medicine	Present Day Therapy and Its Physiologic Basis [95]	November 9-13, full time	30.00 members 60.00 non-members
	TROPICAL MEDICINE		
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	735-A Tropical Medicine	January 4-February 19, full time	300.00
	UROLOGY		
College of Medical Evangelists, 312 N. Boyle Ave., Los Angeles 33, Calif.[42] At: Ambassador Hotel, Los Angeles	General Urology	January 6-March 3, once weekly, part time	35.00
	Genito-Urinary Disease	November 16-20, full time	60.00
Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington 12, D. C.	Postgraduate Seminar in Urology [49,50,51]	September 7-9, full time	None
Cook County Graduate School of Medicine, 707 S. Wood St., Chicago, Ill.	Intensive Course in Urology	September 28, 2 weeks, full time	225.00
Iowa Academy of General Practice, 912 Equitable Bldg., Des Moines, Iowa At: Hotel Warden, Fort Dodge	Urology-Medicine	November 12, 1 day, full time	Non-members 5.00 members free
State University of Iowa College of Medicine, Iowa City, Iowa At: University Hospital	Postgraduate Conference	Monthly, 1st and 3rd Wednesday, part time	None
American Urological Association, 1120 N. Charles St., Baltimore, Md. At: Los Angeles, Calif.	Postgraduate Seminar in Urology	November, 5 days, full time	75.00
New York Polyclinic Medical School and Hospital, 345 W. 50th St., New York 19, N. Y.	Urology	October 1, 8 months, full time	800.00
	Instrumental Urology	Arranged, 4 weeks, part time	75.00
	Operative Surgery for Specialists	Arranged, 2 months, part time	150.00
New York University Post-Graduate Medical School, 477 First Ave., New York 16, N. Y.	672-A Urology (Graduate Course)	September 28-June 18, full time	700.00
	674-A Refresher Course in Basic Urology	November 16-20, full time	60.00

References will be found on page 647.

Postgraduate Continuation Courses for Physicians—July 1, 1953, to Jan. 15, 1954—Continued

Institution	Title of Course	Schedule of Course	Registration Fee and/or Tuition
UROLOGY—Continued			
Oswald Swinney Lowsley Medical Group, 111 E. 71st St., New York 21, N. Y. At: St. Clare's Hospital	Urological Diagnosis and Treatment	1 year, full time	$750.00
American Urological Association, Suite 9B, Doctors' Building, Charlotte, N. C. At: New Orleans, La.	Postgraduate Seminar in Urology	Fall, 5 days, full time	60.00
Hillcrest Medical Center, Twelfth St. and Utica Ave., Tulsa, Okla.	Urology (Seminar and Bedside Rounds)	Arranged, once weekly, part time	None
University of Pennsylvania Graduate School of Medicine, Philadelphia 4, Pa.	Urology [48]	September 28-May 22, full time	960.00
VENEREAL DISEASE			
Public Health Service, Washington 25, D. C.[49] At: Hot Springs National Park	21st V. D. Postgraduate Course	October 12-16, full time	None
Wayne University College of Medicine, 1512 St. Antoine St., Detroit, Mich. At: Receiving Hospital	Conference on Venereal Disease	September 14-December 5, December 7-March 13, 12 weeks, once weekly, part time	15.00

Sponsoring and Contributing Agencies

1. Medical Society of the County of Kings and State University of New York College of Medicine.
2. Arthritis Rheumatism Foundation.
3. Maryland Heart Association.
4. Minnesota Heart Association.
5. The Endocrine Society, Oklahoma City.
6. Nebraska State Medical Society, Lincoln and Nebraska State Department of Health, Lincoln, and University of Nebraska Extension, Lincoln.
7. University of Minnesota Medical School.
8. Institute of Industrial Health.
9. Public Health Service, Division of Occupational Health, Cincinnati, and Department of Dermatology, University of Cincinnati.
10. Kansas State Medical Society and Kansas State Board of Health.
11. Institute of Industrial Health and University of Michigan Law School.
12. Colorado Division of the American Cancer Society.
13. Oregon Chapter of the American Cancer Society.
14. Arkansas State Medical Society and the Arkansas Academy of General Practice.
15. Connecticut State Medical Society.
16. Medical Association of Georgia and Georgia Academy of General Practice.
17. University of Illinois College of Medicine, Stritch School of Medicine and Chicago Medical School.
18. Committee on Postgraduate Education, Massachusetts Medical Society.
19. Wyeth, Inc.
20. Cancer Association, Heart Association and Tuberculosis Association.
21. North Carolina State Board of Health.
22. South Carolina Academy of General Practice and the Alumni Association of the Medical College of South Carolina.
23. Tennessee Academy of General Practice.
24. Dallas Southern Clinical Society.
25. Washington State Medical Association and Washington State Department of Health
26. Chicago Medical Society.
27. Marquette University School of Medicine.
28. Joint Committee of State Mental Hospitals and State Department of Mental Health.
29. Menninger Foundation and Veterans Administration Hospital, Topeka.
30. Kansas State Obstetrical Society and Kansas State Medical Society.
31. Puerto Rico Department of Health.
32. Stanford University School of Medicine.
33. Colorado Ophthalmological Society.
34. Temple University School of Medicine.
35. Puerto Rico Health Department and University of Puerto Rico School of Medicine.
36. Institute of Physical Medicine and Rehabilitation.
37. National Foundation for Infantile Paralysis.
38. Minnesota Trudeau Society and the Minnesota Chapter of the American College of Chest Physicians.
39. Adirondack Counties Chapter of the New York State Academy of General Practice.
40. Ohio Trudeau Society, Ohio Tuberculosis and Health Association and Ohio State Medical Association.
41. U. S. Atomic Energy Commission.
42. Los Angeles Urologic Research Convention.
43. Arkansas State Board of Health.

Footnotes

44. No fee for interns and residents of either hospital. No fee for staff members of San Diego County Hospital. $50 fee for Mercy staff members including physiology course.
45. Designed to prepare candidates for the anatomy examination of the American boards of general surgery and the surgical specialties.
46. Surgery $910.00.
47. Leading to degree of Master of Medical Science in surgery, medicine, obstetrics and gynecology, anesthesiology, otolaryngology, pediatrics, radiology and urology.
48. Formal basic science course in preparation for specialty board certification.
49. Attendance is encouraged from the following individuals:
    a. Medical Corps officers of the Armed Forces on active duty.
    b. Medical Corps officers of the Armed Forces not on active duty.
    c. Physicians from other federal agencies.
    d. Other civilian physicians desiring to attend.
50. Application procedure. Applications should be forwarded so as to reach the addressees listed below not later than six weeks prior to the opening date of the course:
    a. Applications from Army Medical Corps officers on active duty and full time Civil Service physicians on duty at Army installations will be forwarded to the Office of the Surgeon General, Department of the Army, Washington 25, D. C. Attention: Personnel Division, Career Management Branch.
    b. Applications from Army Reserve Medical Corps officers not currently on active duty will be forwarded through channels to the Army Area Commander.
    c. Applications from National Guard medical officers should be forwarded through channels to the National Guard Bureau, Washington 25, D. C.
    d. Applications from medical officers from other branches of the Armed Forces should be forwarded through regularly established channels.
    e. All other applications should be forwarded to the Commander of the installation conducting the course.
51. Course is designed for attendance by individuals who are board qualified and/or board certified, chiefs or assistant chiefs of services, and others well advanced in the study of this specialty.
52. Course is designed for attendance by individuals partially qualified in the specialty or officers responsible for medical treatment in this specialty.
53. Physicians in Cleveland area and interns and residents, no charge. Physicians outside Cleveland area $40.00.
54. July 6, July 20, August 3, August 17, September 14, October 12, October 26, November 9, November 30.
55. Formal basic science course.
56. $125.00 per quarter; $12.00 per week for short periods.
57. Scholarships for tuition available through State Chapters of American Cancer Society in Idaho, Montana, Oregon and Alaska.
58. No fee for interns and residents.
59. Military officers, no fee.
60. Address: Dr. W. M. Dabney, Secretary, Crystal Springs, Miss.
61. Registration fee only. Full time faculty members of Creighton and University of Nebraska medical schools, residents and interns of Omaha hospitals are guests of the Society without payment of registration fee. Senior medical students of Creighton and University of Nebraska medical schools attend all sessions as curricular requirements.
62. Certificate of completion of course granted by University of Oklahoma School of Medicine.
63. Alumni $25.00; non-alumni $75.00; students matriculating in Graduate School of Medicine on September 28, 1953, $15.00.
64. This course is available only to physicians certified.
65. An acceptable thesis leads to the degree of Master of Medical Science. Program is specifically designed to accommodate the candidate for specialty board certification. Credit for one year in lieu of a hospital residency year will be given by certain specialty boards for this course.
66. Colorado, Utah, New Mexico, Montana and Wyoming.
67. Open only to physicians who have been formally approved and accepted for training in psychoanalysis by the Admissions Committee of the Los Angeles Institute for Psychoanalysis.
68. Formal basic science courses in clinical neurology, neuroanatomy, neurophysiology, neuropathology, neuroroentgenology and electroencephalography.
69. Preparation for certification by the American Board of Neurology and Psychiatry.
70. A special short course designed primarily for staff members of mental institutions. Emphasis on neurology.
71. Members of State Obstetric and Gynecologic Society, no fee.
72. Including manikin obstetrics and operative gynecology (cadaver).
73. Includes 1 week course in audiology, fee $100.00.
74. Basic course—1 week, $100.00; clinical course—1 week, $75.00.
75. Except July and August.
76. In preparation for specialty board examination.
77. Basic ophthalmology No. 488, clinical and pathology No. 501, refraction and motor anomalies No. 504.
78. Including cadaver, eye, ear, nose and throat and refraction.
79. Including cadaver ophthalmology and refraction.
80. For four days, $25.00, either part.
81. Fully accredited by the American Board of Orthopedic Surgery.
82. Designed to aid in meeting the requirements of the examination of the special board in neurological surgery.
83. Course approved for board certification.
84. $2.00 per lecture; $15.00 for series of 8 lectures.
85. No fee for interns and residents of either hospital. No fee for staff members of County Hospital. $50.00 fee for Mercy staff members including anatomy course.
86. Registration fee.
87. Leading to the Master of Public Health Degree.
88. $300.00 for nonresidents.
89. Designed primarily for individuals doing research or teaching in field of public health and preventive medicine.
90. Nonmembers pay $1.50 per course or a maximum of $5.00. No charge for graduate students of radiology and members of the American Roentgen Ray Society.
91. July 6, August 3, September 14, September 28, October 12, October 26, November 9, December 7.
92. Including cadaver surgery and gynecology.
93. Including general surgery, orthopedic surgery and physical medicine.
94. Certificate of completion of course granted by University of Oklahoma School of Medicine.
95. For specialists.

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MISCELLANY

THE DISTRIBUTION AND USE OF GAMMA GLOBULIN

Poliomyelitis.—Reports by Hammon and his associates (THE JOURNAL Oct. 25, 1952, and April 11, 1953) are available on the epidemiological studies that form the basis for the use of gamma globulin in the prophylaxis of paralytic poliomyelitis. The children investigated ranged in age from 1 to 11 years and the doses used were 4, 7, or 11 cc., depending on the weight of the child. The average dose approximated 0.14 cc. per pound of body weight.

Significant protection was demonstrated from the second through the fifth weeks following injection and diminishing protection was evident from the sixth to the eighth weeks. There was no significant difference in the number of cases of poliomyelitis in the treated and control groups in the week following injection, but there was evidence of mitigation of paralysis in the cases occurring in the children who had received gamma globulin. This evidence is the basis for the conclusion that gamma globulin will be most effective if given shortly before or as soon as possible after infection. It is of no value after clinical symptoms of the disease have become apparent.

Criteria for Diagnosis.—It will be noted that the basis for allocation to the states depends on the reported incidence of the disease, with the suggestion that the incidence of paralytic cases may be used as a control in making additional and supplemental allocations.

To insure uniform reporting it has been suggested that physicians and health departments adopt criteria for diagnosis similar to those formulated by the National Conference on Recommended Practices for the Control of Poliomyelitis. Following is an excerpt from the suggested criteria:

"Diagnostic criteria of paralytic or non-paralytic poliomyelitis should generally include three or more of the following:

(1) history compatible with poliomyelitis
(2) fever
(3) stiff neck and/or stiff back
(4) 10 to 500 cells per cc. of spinal fluid taken during the acute or early convalescent period of the disease
(5) spinal fluid protein elevated above normal limits
(6) demonstrable muscle weakness or paralysis

"Cases which present only (1) history compatible with poliomyelitis, and (2) fever, should be classified as presumptive, (abortive) poliomyelitis.

"Paralytic cases are defined as those in which definite weakness or paralysis has been detected and persisted during at least two examinations made at intervals of at least several hours. Results of an examination for paralysis of muscles of the extremities or trunk may be very unreliable during the period of muscle tenderness or 'spasm.'"

Gamma Globulin.—Gamma globulin is the name given to one of several fractions of the protein component of human plasma. It is comparable with the product officially known as immune serum globulin. Gamma globulin is prepared commercially by a method involving a series of precipitations with varying concentrations of alcohol under controlled conditions of acidity and low temperature. An average donation of blood (500 cc.) yields 7 cc. of a 16% solution of gamma globulin. This represents a single recommended dose for the prophylaxis of poliomyelitis in a 50 lb. (6 to 7-year-old) child. The production capacity of existing fractionating plants is limited.

Gamma globulin is available as a 16% solution. This solution is opalescent and somewhat viscous, necessitating injection through a no. 18 or 20 needle for quantities required for the prophylaxis of poliomyelitis. Injections should be made intramuscularly, using a separate syringe and needle for each subject. Gamma globulin should never be given by the intravenous route.

The use of separate syringes is recommended because of the danger of contamination of the syringe with blood containing the virus of homologous serum hepatitis. This may occur when one attempts to withdraw blood in order to be certain that the needle point is not in a vein. No instance of hepatitis has been recorded following the use of gamma globulin that has been prepared and administered in the manner described.

Intramuscular injection of gamma globulin is not accompanied by any significant reactions. The danger of local or systemic reactions must, however, be considered if repeated injections are contemplated.

Excerpts from a statement by the Division of Medical Sciences of the National Research Council, dated April 20, 1953.

MEDICAL MOTION PICTURES

Food as Children See It: 16 mm., color, sound, 18 minutes. Produced in 1952 by and procurable on loan or purchase from General Mills, Inc., Film Department, 400 Second Ave., S., Minneapolis.

This film pictures a talk by Dr. Mirian E. Lowenberg, head of the department of foods and nutrition, Pennsylvania State College, to mothers of preschool children. The talk is limited to the presentation of food as preschool children see it. It does not attempt to answer all problems concerned with child feeding. The mothers are urged to serve foods from each of the Basic Seven food groups every day. Dr. Lowenberg points out that foods should be colorful, simple, and appealing to the eye. A good variety of foods with an occasional surprise, such as fruit hidden in custard, is preferable. Lots of finger foods are in order for the children of this age. Emphasis is also placed on maintaining a cheerful atmosphere during mealtime. Children should be encouraged to relax just before eating, and mealtime conversation should remain happy and cheerful. The photographic quality is good; however, the sound quality is below average. This motion picture is a good point of departure around which a discussion could be built. It is suitable for showing at well child conferences and in conjunction with preschool mothers' clubs. Pediatricians could see it for giving discussions before clubs.

Personal Hygiene for Boys: 16 mm., color, sound, showing time 10 minutes. Produced in 1952 by and procurable on purchase ($100) from Coronet Films, 65 E. South Water St., Chicago 1, and on rental from Ideal Pictures Corporation, 58 E. South Water St., Chicago 1, or your local film library.

As the title indicates, this is a film covering certain of the personal hygiene aspects of daily living for boys. It emphasizes cleanliness of the skin, hair, nails, and teeth, beginning procedures in shaving, and other similar items. To a lesser degree, pointers are given on exercise, proper diet, and certain safeguards against becoming infected by common diseases. The motivation of the film should appeal strongly to teen-age youngsters who desire to present a good appearance and to build strong, healthy bodies. The picture is attractive and well done. The photographic and sound quality are very good. It should be of greatest use at junior and senior high school levels and may have wider application in youth groups and clubs. A study guide is available from the producer.

Personal Health for Girls: 16 mm., color, sound, showing time 10 minutes. Produced in 1952 by and procurable on purchase ($100) from Coronet Films, 65 E. South Water St., Chicago 1, and on rental from Ideal Pictures Corporation, 58 E. South Water St., Chicago 1, or your local film library.

Emphasis is given to cleanliness as a means of maintaining good health and appearance. The film covers such topics as care of the teeth, hair, and skin; proper eating habits; adequate rest; exercise; and the importance of clean clothing. Safeguards against infection are briefly covered, along with the appropriate use of cosmetics and personal hygiene pointers on menstruation. The photographic and sound quality are very good. The film is suitable for persons of junior and senior high school ages. A study guide may be obtained from the producer.

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*Effects of Banthine on Pain and Antral Gastric Motility in Patients with Duodenal Ulcer. N. C. Hightower Jr. and E. E. Gambill.—p. 244.
*Mechanism of Pain in Peptic Ulcer. J. M. Ruffin, G. J. Baylin, C. W. Legerton Jr. and E. C. Texter Jr.—p. 252.
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Use of Oral Procaine in Case of "Lysol" Poisoning. A. D. Silk and S. J. Stempien.—p. 301.
Incidence of Coexistence of Gastric and Duodenal Ulceration. M. Feldman.—p. 304.

Anticholinergic Drugs and Gastric Secretion.—The effects on gastric secretion in man of six anticholinergic drugs, namely, methantheline (Banthine), "prantal" (N,N, dimethyl-4-piperidylidene-1,l-diphenyl-methane methyl sulfate) and four new preparations designated as AP-193 (diethylaminoethyl beta hydroxy alpha phenyl cyclohexane acetate), U-0407 (pyrrolidyl ethyl phenylcyclopentenyl acetate etho-bromide), U-0385 (diphenyl-[2-piperidyl ethyl] acetamide methobromide), and U-0229 (alpha, alpha-diphenyl-gamma-[1-piperidyl]-butyramide hydrochloride) were compared. The authors' studies were limited to patients secreting acid gastric juice continuously under basal conditions. The stomach was aspirated continuously, the contents being collected every 15 minutes; the volume and free acidity were measured for each specimen. Each test was continued for approximately three hours or until the original levels were regained. The effects of the drugs on basal secretion were investigated in a total of 359 experiments, with the compounds administered intramuscularly in 165, orally (by gastric tube) in 176, and intraduodenally in 18. The occurrence and severity of side-effects were estimated by inquiry concerning appropriate symptoms and by the following measurements: output of saliva, degree of mydriasis and the pulse rate and blood pressure. The influence of U-0385 and U-0229 on the nocturnal and the 24-hour secretion was studied in a small group of patients. The continuous gastric secretion before, during and after the intravenous infusion of U-0229 was measured in seven patients with duodenal ulcer. The effects of methantheline, "prantal," U-0407, U-0385 and U-0229 on gastric secretion stimulated with a histamine analogue (3-beta-aminoethylpyrazole) were investigated in 34 experiments. Compounds U-0229, U-0407, methantheline and "prantal," listed in their order of potency, suppressed basal gastric secretion temporarily when given intramuscularly in sufficient amounts. Only U-0229 and U-0385 inhibited the free acidity consistently after oral administration. Compounds U-0407, methantheline and "prantal" decreased gastric acidity only occasionally after oral administration; AP-193 was totally ineffective. The intravenous infusion of 6 to 11 mg. of U-0229 induced prolonged anacidity in the majority of a group of patients with duodenal ulcer. Compounds U-0229, U-0385, U-0407, methantheline and "prantal" delayed, but did not suppress, the gastric secretory response to 3-beta-aminoethylpyrazole. The three anticholinergic drugs tested, U-0407, U-0385 and U-0229, did not inhibit secretion maximally stimulated with repeated injections of 3-beta-aminoethylpyrazole. The frequency and duration of anacidity increased, generally, though not exclusively, in proportion to the incidence and severity of side-effects. The most potent antisecretory compounds, U-0229 and U-0385, produced symptoms such as dryness of the mouth and throat, blurring of vision and delay in urination, more often than less effective compounds.

Effects of Methantheline on Pain and Motility.—The effects of methantheline (Banthine) bromide on the pain of duodenal ulcer and on antral gastric motility in 8 men and 4 women between the ages of 25 and 54 with this disease were studied. In preparation for the study, all patients were fasted from 14 to 16 hours, during which time all medication was stopped. Antral gastric motility was recorded by a balloon-photokymographic technique with the patient reclining flat in the supine position on a comfortable bed. Pain was registered on the photokymograph by means of a light signal activated when the patient pressed a small hand switch. After a control period of observation of approximately one hour, methantheline in a dose of 100 mg. was administered orally with about 15 cc. of tap water. The recording was then continued for approximately another hour. While the complete mechanism for the production of pain of duodenal ulcer is not clear the present study revealed that in those patients with an intermittent type of pain there was a positive correlation between the occurrence of type 2 antral contractions (phasic pressure waves of the gastric antrum) and the subjective evidence of pain. Methantheline was thus found to be an effective agent for inhibiting type 2 antral contractions in patients with duodenal ulcer and produced results similar to those observed previously in a group of patients with duodenal ulcer who had undergone vagotomy.

Mechanism of Pain in Peptic Ulcer.—In studying the mechanism of ulcer pain, at least two factors must be considered, namely, hydrochloric acid and gastric motility. Since both of these are variables, it is impossible to evaluate the effect of either factor upon ulcer pain without controlling the other. In the authors' study the acid values were artificially raised to the high levels usually associated with ulcer pain, by administering orally 200 cc. of 0.1 normal hydrochloric acid to 88 patients

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Titles marked with an asterisk (*) are abstracted.

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having an active ulcer with typical pain within the preceding 24 to 48 hours. In this manner the role of the remaining variable, motility, could be correctly appraised. In 66 patients 2 oz. (60 gm.) of barium sulfate were added to the hydrochloric acid and the patients observed fluoroscopically at frequent intervals for a period of 30 minutes. Determinations of gastric acidity before and after the administration of acid and of the suspension of acid and barium were made in 25 patients. Despite high acid values, only 37 of the 100 "acid tests" performed on the 88 patients produced pain. From this observation alone the concept that hydrochloric acid per se is the cause of ulcer pain can be questioned. On the contrary, the authors' studies indicate that ulcer pain in the uncomplicated case is invariably associated with abnormal motility. Pain appeared with the onset of abnormal motility and ceased when motor function returned to normal. This abnormality consisted of incoordinated activity of the antral evacuation mechanism with or without localized spasm. The 39 patients with negative tests on whom detailed fluoroscopic observations were carried out showed none of these abnormalities. Most of them showed normal motility with prompt evacuation. The remainder had quiet inactive stomachs with a patent pylorus, and gastric emptying proceeded normally when the patient was placed in the recumbent right anterior oblique position. The use of drugs affecting motility afforded further opportunity for studying the relationship of ulcer pain and motility. Twenty-six patients were given methantheline or a new cholinergic blocking agent (SKF-1637), with prompt relief of pain in 25. This coincided exactly with cessation of abnormal motility and relaxation of the stomach. From these observations the concept is advanced that abnormal motility is the fundamental mechanism through which ulcer pain is produced. For the production and perception of ulcer pain, there must be (1) a stimulus (hydrochloric acid or others less well understood); (2) an intact motor nerve supply to the stomach and duodenum; (3) altered gastroduodenal motility; and (4) an intact sensory pathway to the cerebral cortex.

GP (J. Am. Acad. Gen. Practice), Kansas City, Mo.

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*Carbon Dioxide Inhalation Therapy of Neuroses. J. D. Moriarty.—p. 181.
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Carbon Dioxide Inhalation Therapy of Neuroses.—Over a three year period approximately 6,200 carbon dioxide inhalation treatments were administered to 213 patients with various psychoneurotic conditions. Using an anesthesiologist's gas machine, Moriarty administered a mixture of 30% carbon dioxide and 70% oxygen. The author's method, which represents a modification of Wilcox's technique, permits the patient to reach a deep level of anesthesia without a protracted period of hyperventilation. Usually after 25 to 40 respirations the patient reached a sufficient level of coma, and the mask was then removed; he waked within 40 to 60 seconds after the removal of the mask. The whole inhalation procedure may be administered in approximately five to six minutes. In order to facilitate the therapeutic process, two or more carbon dioxide treatments were administered to many patients during a therapeutic session, allowing about 10 minutes for rest and psychotherapeutic interviewing between the inhalation procedures. Results obtained in the first 66 patients are analyzed in some detail and seem representative of the total group of 213. Of the 66 patients, including seven nosological groups, namely, anxiety neuroses, character neuroses, psychosomatic reactions, alcoholics, homosexuals, depressive reactions and conversion hysterias, 26 (39%) were much improved, 28 (43%) were improved, and 12 (18%) were therapeutic failures. The fact that some patients made an excellent response with as few as 8 treatments and others required 70 or 80 treatments before showing a sustained improvement of equal degree indicates the tremendous variability of response to carbon dioxide therapy and emphasizes the need for adequate treatment. As a result of his experience the author states that carbon dioxide inhalation therapy produces favorable effects in many anxiety states and phobic reactions, some character neuroses, certain psychosomatic conditions like spastic colitis and migraine headaches, and some alcoholic problems. It is usually very desirable to utilize psychotherapy in close conjunction with this neurophysiological treatment. The neurophysiological action of the carbon dioxide on the nerve cell is to raise the membrane potential, which in turn raises the threshold of stimulation of the nerve, decreases the speed of conduction of impulses, and increases the height and prolongs the duration of the action potential. The central effects of carbon dioxide include a pronounced increase of cerebral blood flow, increase in the respiratory rate and oxygenation of the blood, and a shift of the cortical pH to the acid side. In general, carbon dioxide first inhibits the higher (cortical) centers and releases the lower (brain stem) centers. Secondarily, the latter are inhibited in progressive fashion, in reverse order of their phylogenetic development. The healing mechanisms of carbon dioxide therapy are not clearly understood but probably involve a breaking up of pathological reverberating circuits in the nervous system, thereby allowing the homeostatic mechanisms of the organism to take over again. In addition, emotional tensions are released and unconscious material becomes more accessible, facilitating the psychotherapeutic process.

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*Physiological Effects of Operations for Duodenal Ulcer. R. H. Smithwick. —p. 77.
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Physiological Effects of Operations for Duodenal Ulcer.—The physiological aim of the surgical treatment of duodenal ulcer is to reduce the digestive power of the gastric juice, but while Wangensteen believes that to accomplish this, achlorhydria to stimulation by histamine is desirable, Dragstedt feels that reducing the amount of acid production to within the normal range is sufficient. In evaluating these points of view Smithwick describes the method he uses to determine the gastric acidity of ulcer patients. A Levin tube is placed with the tip at the mid-point of the stomach or gastric remnant under fluoroscopic control. Gastric juice is collected for one hour by continuous suction, the subject having fasted overnight; this is the basal test. Then 80 cc. of peptonized beef broth is introduced into the stomach and aspirated after 20 minutes. The gastric contents are again aspirated for a one hour period; this is the broth test. Fifteen units of insulin are then injected intravenously. Blood sugar levels are obtained before and at half-hour intervals over a two hour period following the administration of insulin. Gastric juice is aspirated by continuous suction until two one-hour samples are obtained. The free acid values for all four one-hour specimens are determined by electrometric titration to a pH of 3.5. The pH of each specimen is also recorded. The specimen that contains the largest amount of acid following the injection of insulin is taken as the response to vagal stimulation; this is usually the second of the two one-hour specimens. The early physiological effects of various operations for duodenal ulcer were determined according to the described method. Wide variations were found. Recurrent ulceration does not occur if achlorhydria is present in the fasting stomach, following a potent food stimulus and after vagal stimulation as well. The only operations which can be depended upon to consistently produce achlorhydria under these circumstances are those involving resection of at least the distal one-half of the stomach together with the vagus nerves. There appears to be a close relationship between the more serious untoward side effects of operations for duodenal ulcer and the size of the gastric remnant. The best clinical results are obtained by patients having the larger gastric remnants. Since the physiological effects of hemigastrectomy combined with resection of the vagus nerves compare favorably with those following operation involving the removal of a larger portion of the stomach, and since the clinical results are superior, this procedure is more likely to supplant subtotal gastrectomy alone than any other procedure studied to date.

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Acute Osteomyelitis of Maxilla in Infancy. C. R. McCash and N. L. Rowe.—p. 22.
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Lipoma Causing Posterior Interosseous Nerve Lesion. D. A. Richmond. —p. 83.
Hydatic Cysts of Femur: Total Removal of Femur and Replacement by Complete Cadaveric Femur. R. G. Capurro and P. V. Pedemonte. —p. 84.
Osteopathia Striata—Voorhoeve's Disease: Report of Case Presenting Features of Osteopathia Striata and Osteopetrosis. R. L. Hurt.—p. 89.
Cervical Hyperextension Injuries with Paraplegia. C. J. Kaplan.—p. 97.
An Unusual Bone Tumour Complicating Paget's Disease. D. M. T. Cones.—p. 101.
Familial Paget's Disease with Early Onset. R. E. Irvine.—p. 106.

Journal of Pathology and Bacteriology, Edinburgh

65:1-278 (Jan.) 1953. **Partial Index**

Congenital Fibro-Elastosis of Endocardium. N. F. C. Gowing.—p. 13.
Reticular Tissue and "Reticulo-Endothelial System." A. H. E. Marshall. —p. 29.
Stimulation of Haemolysis by Penicillin. P. Story.—p. 61.
Demonstration of Tubercle Bacilli in Milk. H. W. Smith.—p. 67.
Schumann Bodies in Tuberculous Salpingitis. J. C. Burne.—p. 101.
*Structural Changes Around Nails and Screws in Human Bones. D. H. Collins.—p. 109.
Ground Substance of Fibrous Tissue in Experimental Liver Cirrhosis. M. Balasubrahmanyan.—p. 123.
Histogenesis of Adenolymphoma of Salivary Glands. J. D. Hicks.—p. 169.
The L Form Bacteria in Relation to Antibiotics. R. J. V. Pulvertaft. —p. 175.
Struma Reticulosa: Reconsideration of Undifferentiated Tumours of Thyroid. D. B. Brewer and J. W. Orr.—p. 193.

Structural Changes Around Nails and Screws in Bones.—The changes taking place around intraosseous stainless-steel nails were studied in 12 instances of fractures of the neck of the femur from six days to five years after operation. The entry of the nail shatters a few trabeculae and causes a small amount of hemorrhage within the bone. The repair of this damage leads to the encapsulation of the nail by fibrous tissue, which forms a smooth membranous lining to the nail track. This is well developed in five or six weeks, and new bone appears in the fibrous wall about the same time. Further bone deposition in the fibrous tissue and pre-existing trabeculae forms, in 20 weeks or over, a more or less continuous bony shell around the nail track. This new bone gradually becomes consolidated, and at 2½ years plates of lamellated bone are seen which at five years are endowed with Haversian systems and then resemble true bone cortex, continuous around the lip of the track with the external cortex of the femur and covered by a layer of fibrous tissue continuous with the external periosteum. Stainless steel containing 18% of chromium and 8% of nickel appears to be noncorrodible and inert in human tissues. Screws were used to secure steel plates along the femoral shaft in some of the aforementioned cases in which nails had been used for the fractured femoral neck. The region of the screw holes was examined histologically in two cases 11 days and 5 weeks, respectively, after operation. The tissue reaction around the screws seems to resemble that around the three-flanged nails, so far as the medullary tissues and the intramedullary course of the screws are concerned. The absence of reaction in the cortical tunnel may be in part explained by the scarcity of vascular connective tissues from which the repair tissue could spring, but also the cortical bone and the cellular tissues within the Haversian canals in the immediate vicinity of the screw hole are dead, killed no doubt, as Watson-Jones stresses, by heat from the high-speed mechanical drill used to prepare tracks for screws through compact bone.

Nordisk Medicin, Stockholm

49:121-160 (Jan. 23) 1953. **Partial Index**

*Dicumarol Intoxication, Its Prophylaxis and Therapy. O. Z. Dalgaard. —p. 121.
Operative Treatment of Varices: Follow-up Examination of 1944 Material from Surgical Department of Södersjukhus. E. Arenander.—p. 129.
Urea Tolerance Test as Liver Function Test. M. Yli-Pohja.—p. 133.
Nephrotic Syndrome After Treatment with Tridione. K. A. Steffensen and S. Brandt.—p. 134.
Bronchial Cancer Following Massive Inhalation of Gasoline. A. C. Julsrud.—p. 136.

Prophylaxis and Therapy of Bishydroxycoumarin Poisoning.—Dalgaard tabulates from the literature 80 deaths from hemorrhage during anticoagulation treatment with bishydroxycoumarin (Dicumarol). The hemorrhage in most serious cases is localized to the regions with pathological changes, and exact diagnosis before the start of anticoagulation treatment is therefore important. The contraindications to the use of bishydroxycoumarin are essentially those laid down by Allen. The treatment has been considered as contraindicated in renal insufficiency, but Sachs has treated nine patients with chronic renal insufficiency with bishydroxycoumarin in ordinary doses without any unusual effect; he warns against the use of bishydroxycoumarin in cases with anuria and in more marked hematuria. The most important contraindication is lack of adequate and reliable laboratory control. Owren's method is recommended for control of bishydroxycoumarin treatment. The dosage must be individualized on the basis of the patient's reaction to a fixed initial dose and must, if necessary, be varied throughout the treatment. The average daily dose for maintenance of prothrombin concentration within the optimal therapeutic limits (between 10 and 20 to 30%) is 50 to 60 mg. Some patients tolerate only about 30 mg. daily; others, more resistant, tolerate up to 125 mg. daily. Bishydroxycoumarin treatment has hitherto largely been carried out as an intermittent treatment, with relatively large doses at intervals of a day or possibly several days; a more even effect is reached by small doses given daily. In simple vitamin K deficiency, as in obstructive jaundice and in hemorrhagic diathesis in the newborn, about 5 mg. of menadione bisulfite is sufficient. It is thought that vitamin K_1 should be applied in all cases where the prothrombin activity is to be increased as rapidly as possible, but where it is desirable to increase the prothrombin activity only to the therapeutic level the synthetic preparations are preferable. A single dose of 500 mg. vitamin K_1 given orally acts almost as rapidly and effectively as the same dose intravenously except in patients who vomit or have gallbladder fistula or gallbladder drainage. Blood transfusion is of some value but seldom necessary unless there has been massive hemorrhage, when the purpose is rather to compensate for the blood lost than for the prothrombin.

Presse Medicale, Paris

61:125-144 (Jan. 31) 1953. **Partial Index**

Mechanism of Cardiovascular Collapse Occurring in Course of Certain Disorders in Upper Abdominal Region. R. Gueullette.—p. 125.
Action of Cyclo-Hexyl-1-Phenyl-Pyrrolidine-3-Propanol-1 Hydrochloride on Symptoms of Parkinson's Disease; Comparative Study with Other Therapeutics. J. Sigwald.—p. 127.
*Physiology of Organism Subjected to Deep Cooling. J. Giaja.—p. 128.

Physiology of Organism Subjected to Deep Cooling.—As a result of his experiments performed on rats, the author states that it is possible to cool a homothermal animal by placing it in an air-tight jar, which then is immersed in ice-cold water, i. e., by withdrawing from the animal more heat than it can produce in its extreme fight against the cold. The term "direct forcing by external cold" is used to describe this technique. When the oxygen pressure of the inhaled air is reduced below a certain value, the intensity of the intraorganic combustion becomes a dependent variable of this pressure; below a certain preliminary pressure, hypothermia runs an equal course with the depression. The atmosphere in the air-tight jar grows poorer

and poorer in oxygen, whereas it gets richer in carbon dioxide. Under the effect of the resulting hypoxia and hypercapnia, the closed-in animal grows gradually colder and within one and a half to two hours its rectal temperature drops to 15 C (59 F). At this stage the animal is thoroughly anesthetized. It has become a poikilothermal, because it does not show any tendency to increase its temperature when it is placed again in the open air at an external temperature of 15 C (59 F). The animal is able to live for 20 hours in this condition of experimental poikilothermism, a true physical anesthesia, which has been used currently for physiological operative experiments. Due to the low blood pressure there is very little bleeding and the risk of asphyxia is considerably diminished. The animals whose temperature had been reduced to 15 C recovered completely by external warming even after several hours of poikilothermism. There were no immediate or late undesirable side-effects. Cooling for one hour could be repeated 20 times in the course of one month. Three stages were distinguished in the course of cooling as follows: the initial stage of hypothermia during which the animal's temperature is not lower than 20 C (68 F) and there is excess oxidation; the second phase of cooling, for which the term experimental poikilothermism has been coined, occurring between body temperatures of 20 C and 15 C (in this phase the rat resembles the frog in its reaction to hypothermia); the third stage of physical anesthesia is reached at a temperature of about 15 C. If the cooling is continued below 15 C, first respiration ceases (stage of apparent death), and if the temperature is still further reduced below 8 C (46.4 F), the heart ceases to beat. Observations on hibernating mammals such as the spermophilus (a genus of marmots) suggest that the result of deep cooling in homothermal animals which were thus transformed by the author into poikilothermal animals should be distinguished from the dormant state in which hibernating mammals pass the winter. The hibernating animal is able to warm itself automatically by its own means if the cooling becomes too deep and is then able to offer resistance to temperatures much lower than those that have provoked hibernation. Cooling and warming are active physiological phenomena in the hibernating mammal, but passive phenomena in the author's experimental animals. Despite the fact that deep cooling has been artificial and experimental, it is to be considered as a physiological condition observed in the course of phylogenesis as well as of ontogenesis.

Schweizerische medizinische Wochenschrift, Basel

83:145-170 (Feb. 14) 1953. **Partial Index**

Problems of Interstitial Nephritis. O. Spühler.—p. 145.
*Criteria of Success of Treatment in Pulmonary Tuberculosis. F. Rotach. —p. 148.
Problem of Proteinuria and Its Differential Diagnostic Significance. F. Lasch.—p. 153.

Criteria of Success of Treatment in Pulmonary Tuberculosis.—According to Rotach, results of chemotherapy in pulmonary tuberculosis should be evaluated on the basis of the roentgenologic aspect rather than on single clinical symptoms. Improvement in clinical symptoms frequently may not be accompanied by a parallel morphological regression in the roentgenologic picture. Subjective well-being, increase in body weight, drop in erythrocyte sedimentation rate and decreased amount of sputum may occur fairly regularly under chemotherapy, but should not be considered as a decisive turning point to recovery in the individual case. The disappearance of Mycobacterium tuberculosis from the sputum also is a questionable criterion for the evaluation of the effect of chemotherapy, because disappearance of the bacilli may frequently result from chemotherapy while cavities may remain unchanged. Closure of the lesions can be proved only by negative bacteriological findings and by the simultaneous disappearance of the cavities under thorough roentgenologic control. Cavity closure can be demonstrated by tomography only. Regression of pericavernous infiltration and breaking down of caseous masses in the wall of the cavity may be the results of chemotherapy; thus the formerly clearly visible, circumvallate cavity is changed into a cystic formation with soft walls, which does not render any characteristic shadows on general roentgenologic examination. It is only on tomographic examination that one can decide whether or not closure of the cavity has occurred. Thus medical treatment by the family physician has its definite limitations. Chemotherapy as it is practiced today may in many cases favor the establishment of favorable conditions for recovery, but a sterilization of foci does not result even if the employed drug proves bactericidal in vitro. An anatomic cure of tuberculosis, therefore, cannot result from chemotherapy alone. Collapse therapy, which may frequently be combined with chemotherapy in order to be successful, also creates only better conditions for a cure of tuberculosis. The final course of the tuberculosis depends on the defense powers of the organism, and open-air treatment at a sanatorium, therefore, remains the basic method, which should not be neglected in favor of active purely medical or surgical treatment.

Semaine des Hôpitaux de Paris

29:575-626 (Feb. 15) 1953. **Partial Index**

Common Bile Duct in Pancreatitis. J. Caroli and J. Nora.—p. 575.
Time of Appearance of Sulfobromophthalein in the Bile; New Test for Diagnosis of Incomplete Icterus Due to Retention and Anicteric Blocking of Main Duct. J. Caroli and Y. Tanasoglu.—p. 591.
*Diabetes Mellitus Cured by Laennec's Cirrhosis. J. Caroli, J. Etévé and J. Bertrand.—p. 607.

Diabetes Mellitus Cured by Laennec's Cirrhosis.—According to Caroli and co-workers, the primary role of the diseased liver in the pathogenesis of diabetes mellitus in man has not yet been clinically demonstrated. The occurrence of cirrhosis of the liver associated with ascites is reported in three men, aged 72, 65, and 62, respectively, with diabetes mellitus of more than 10 years' duration. Two of the patients were alcoholics and that suggested the alcoholic origin of the cirrhosis, while the cirrhosis in the third patient was probably secondary to virus hepatitis. Pronounced hyperglycemia as well as glycosuria in the first two patients and hyperglycemia in the absence of glycosuria in the third patient were considerably improved in the course of the cirrhosis. Hyperglycemia did not recur in these patients despite considerable improvement in the ascites as a result of fractional and repeated tapping and a diet containing large amounts of carbohydrates. These observations as well as others collected from the literature suggest that the improvement of diabetes mellitus in the course of an atrophic cirrhosis, mostly due to an inadequate diet in heavy drinkers, is not due to incidental dietetic restrictions in carbohydrates, since it persists despite a high caloric diet rich in carbohydrates. The antidiabetic effect of destruction or removal of liver tissue is further shown by the fact that: (1) removal of the liver in animals at the time of pancreatectomy prevents completely the hyperglycemia that would normally occur after pancreatectomy, and (2) removal of the liver subsequent to pancreatectomy causes a sharp drop in the elevated blood sugar. Hyperglycemia and glycosuria can be artificially produced by cortisone, but this cortisone diabetes does not develop after hepatectomy. The first of the authors' three patients remained in good condition for two years in response to repeated fractional tapping, but within 14 days after the last tapping a pneumococcus peritonitis caused his death. Necropsy revealed that the improvement in the patient's diabetes mellitus was not due to a pronounced decrease in the amount of functional parenchyma, since the lobular parenchyma was fairly well preserved despite annular cirrhosis. Pronounced hyperplasia of the islands of Langerhans involving mainly the beta cells and the observation of a small chromophobe adenoma of the pituitary strongly suggested that the improvement of the diabetes mellitus was related to secondary changes in the endocrine glands and particularly to the hyperplasia of the Langerhans' islands.

Tubercle, London

34:33-66 (Feb.) 1953

Effect of Certain Infectious Diseases on Tuberculin Allergy. J. W. Bentzon.—p. 34.
Place of Chemotherapy in Planned Treatment Regimes for Pulmonary Tuberculosis (Review of 395 Patients). G. F. Edwards.—p. 42.
Sleep and Tuberculosis. B. Benjamin and F. A. Nash.—p. 50.
Rehabilitation of the Tuberculous: Analysis of Results at Remploy Factory, 1949-1952. R. Hardy.—p. 54.

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BOOK REVIEWS

Diseases of Metabolism: Detailed Methods of Diagnosis and Treatment. Edited by Garfield G. Duncan, M.D., Director of Medical Division, Pennsylvania Hospital, Philadelphia. With contributions by Walter Bauer, et al. Third edition. Cloth. $15. Pp. 1179, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1952.

This is a critical appraisal of present knowledge of metabolic processes. The general policy of dealing first with normal and pathological physiology and then with clinical aspects has been maintained in this third edition. The chapters on carbohydrate metabolism, water balance in health and disease, malnutrition, disorders of the thyroid gland, and diabetes in children have been rewritten. The chapter on diabetes has been revised considerably, and much has been added to the chapter on vitamins and avitaminosis. A chapter on porphyrin metabolism has been added. Several chapters, such as the introductory chapter and that on obesity, have been condensed without any apparent loss of value.

The frequent mention of corticotropin (ACTH) and cortisone in the various chapters is evidence of the wide use of these agents. The development of radioactive iodine as a therapeutic and diagnostic agent in evaluating disorders of the thyroid gland has been considered in detail. The importance of the isotope technique in furthering understanding of physiological processes is emphasized. Particular attention has been given to the uses of the various types of insulin, especially the relatively new, modified protamine zinc insulin, in the therapy of diabetes. The use of folic acid and vitamin B_{12} in the problems of primary anemia and the value of vitamin B_{12} in correcting diabetic neuropathies are emphasized. The author allows overlapping of subject material in the chapters on water balance, mineral metabolism, and kidney diseases. Considering the nature of the three subjects, this duplication seems to be wise.

The author and his collaborators have attempted to bridge the gap between the investigator and the practicing physician, and the clinical aspects have been dealt with in fairly comprehensive detail. A discussion of the present status of trace minerals in relation to diseases of metabolism would have been of interest, inasmuch as the general practitioner is flooded with literature by the pharmaceutical houses and others who are incorporating trace minerals in vitamin and mineral supplements. The book should be of interest and of value to any student, investigator, or physician interested in diseases of metabolism.

Unipolar Lead Electrocardiography and Vectorcardiography, Including the Standard Leads, the aV and V Leads, the Cardiac Arrhythmias and the Principles of Vectorcardiography. By Emanuel Goldberger, M.D., F.A.C.P., Associate Attending Physician, Montefiore Hospital, New York. Third edition. Cloth. $10. Pp. 601, with 312 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1953.

The third edition of this widely read textbook is now about three times its original size owing to revisions and additions in the text, and new diagrams and illustrations. An entire section on vectorcardiography has been added, dealing with various methods of obtaining a vectorcardiogram, or deriving it from a routine electrocardiographic tracing. The author includes for the first time his own views on the theoretical aspects of vectorcardiography and describes normal and abnormal vectorcardiographic patterns in correlation with the principles of unipolar electrocardiography introduced in previous editions of the book.

In the sections on clinical aspects of electrocardiography, ventricular strain now fills a complete chapter. A distinction is made between patterns of ventricular strain and those indicating ventricular hypertrophy, and a pattern of acute right heart strain is distinguished from that of acute cor pulmonale. Various clinical conditions associated with electrolyte imbalance, especially hypopotassemia, are described at great length, and the respective electrocardiographic alterations are illustrated. Their importance appears overemphasized when compared with the small amount of attention given to other electrocardiographic abnormalities, such as atypical patterns in myocardial infarction, encountered more often in practice. Considering the additions to the discussion of contour changes, and the many pages and illustrations devoted to detailed description of intricate electrical positions, the section on cardiac arrhythmias is too brief. The author has accepted without hesitation Prinzmetal's views on the mechanisms of auricular arrhythmias. Aberrant ventricular conduction is hardly mentioned in the description of premature beats and in the differential diagnosis of ventricular tachycardia, and the concept of sinoauricular block is completely omitted. The statement that quinidine usually slows the ventricular rate in auricular flutter and the reason given for this contradict all previous experimental and clinical observations.

While the typography of the book is excellent, the technical quality of the numerous illustrations is often poor, especially in some of the new additions. The bibliography is not up-to-date. The book is far too complex for the beginner in electrocardiography and the general practitioner, and is a disappointment for the cardiologist interested in clinical electrocardiography.

Clinical Electrocardiography in Children. By Gertrude H. B. Nicolson, M.D., Associate in Cardiology, Chief of Children's Cardiac Clinic and Assistant Visiting Physician to Children's Service at St. Luke's Hospital, New York. Cloth. $3.25. Pp. 118, with 59 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1953.

The author has not been successful in her stated endeavor "to answer the growing need for a concise and comprehensive work on the subject of the electrocardiogram in the child in health and disease." This is partly because observation of five hundred children is certainly not sufficient basis for such a study. In addition, this material is worked out in a rather superficial way. An extensive discussion and illustration of the changing electrocardiographic pattern in early childhood and in the normal adolescent would be more appropriate than a description of single waves in single leads and of the various electrical positions. Similarly, incomplete and frequently erroneous diagnostic criteria for abnormalities relatively rare in childhood, like myocardial infarction, bundle branch block, and some disturbances of rhythm, are beyond the scope of the book and are dealt with in any text on electrocardiography. The best part of the book is the chapter on congenital heart disease. Unfortunately, here, as in other chapters dealing with abnormalities of the child's electrocardiogram, the poor technical quality of the material, obvious misinterpretations and loose terminology in the legends and text, as well as five different tables of normal rates and P-R intervals, contribute to the reader's confusion.

The Microbiological Assay of the Vitamin B-Complex and Amino Acids. By E. C. Barton-Wright, D.Sc., F.R.I.C. Cloth. $4. Pp. 179, with 25 illustrations. Pitman Publishing Corporation, 2-6 W. 45th St., New York 36; Sir Isaac Pitman & Sons, Ltd., Pitman House, 39-41 Parker St., Kingsway, London, W.C.2, 1952.

This text is English writing at its best. It is clear, simple, thorough, well organized, adequately illustrated, and fully indexed. The work will be doubly welcome to the beginner, because it collects the widely scattered literature, and because it gives detailed directions for each step in each assay. In covering the analyses of 10 B vitamins and 18 amino acids, the author purposely omits vitamin B_{12}, since no published method is considered fully reliable and in most of these only very small volumes of solution of amino acids are used; these techniques are unsuitable for the beginner. Although the book is an introductory text, most workers in the field should read it, particularly the general sections.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

QUERIES AND MINOR NOTES

CONGENITAL MENTAL DEFICIENCY AND STERILIZATION OF PARENTS

To the Editor:—*A young mother has consulted me about terminating her present third pregnancy. Both previous pregnancies resulted in mentally defective children, the condition in each being diagnosed as probable cerebellar ataxia, with mixed dominance. Birth trauma as a causative factor seems unlikely. The physician who attended the woman claims that both deliveries were normal in all respects. In the background of neither mate is there a known similar case. The couple has decided to have the pregnancy interrupted. I am inclined to agree. If this is due to a genetic abnormality, future pregnancies will carry a similar risk. I feel that one parent should be sterilized. What is your opinion?*

Dominic Pellillo, M.D., Tucson, Ariz.

Answer.—The actual causes of congenital mental deficiencies are not known, with few exceptions, such as rubella during the first three months of gestation, erythroblastosis, and radiation treatment during early pregnancy. D. P. Murphy (Congenital Malformations: A Study of Parental Characteristics with Special Reference to the Reproductive Process, ed. 2, Philadelphia, J. B. Lippincott Company, 1947) has shown that recurrence of monstrous children is common. In general, the parents of a congenitally malformed child are about 25 times more likely to produce another defective child than are parents whose children are all normally developed. Furthermore, if two children in a family exhibit congenital defects, there is a 50% chance that the same defect will reappear in a subsequently born brother or sister. In view of the fact that there is at least a 50% chance that a third child will be abnormal, interruption of pregnancy may be justifiable; however, consultation with another physician must be had before the uterus is emptied. Likewise, the question of sterilization in such a case may be considered. Certainly if this pregnancy is permitted to continue and a third defective child is born, sterilization should be carried out on either the husband or the wife. It is far simpler to sterilize the male than the female. Whether this should be done now is debatable, but perhaps it is justifiable. It must be remembered that statistically the baby in utero has almost a 50% chance of being normal.

PREGNANCY IN POSTPOLIOMYELITIC PATIENT

To the Editor:—*Please advise me concerning pregnancy in a postpoliomyelitic patient, with reference to management of the antenatal course and choice of anesthetic for delivery. There is paralysis of both lower extremities, but the patient is ambulant on braces. The circulatory pattern in the legs is poor. There is continence of the urine and feces. The patient's general condition is excellent.*

Gene S. Pierce, M.D., New Albany, Ind.

Answer.—There are many recorded cases of normal labor occurring in women with complete or partial transection of the spinal cord. In general, it may be said that spinal cord lesions do not interfere with the normal activity of the uterus in labor nor do they affect its normal growth in pregnancy. Therefore, in a patient who is postpoliomyelitic, irrespective of the extent of disability, there should be no difficulty from this source, either in the course of pregnancy or in the pattern of labor. Prenatal care should consist only of the ordinary routine precautions, with particular attention to adequate rest and nutrition and avoidance of excessive weight gain. If physiotherapy is being employed, measures permissible during pregnancy include hydrotherapy and active and passive exercises. Massage should be avoided. Labor may be conducted along entirely orthodox lines. Spinal anesthesia is interdicted in a patient who has had any central nervous system lesion or back injury and, therefore, should not be used in this patient. The same is true of caudal anesthesia. Inhalation or local anesthesia is entirely permissible.

SENSITIVITY TO CONTRAST MATERIALS

To the Editor:—*It is customary in some urological departments to test sensitivity to intravenous contrast materials by placing a drop of the solution in the conjunctival sac. In the event the patient is highly sensitive, can the resulting reaction cause ocular damage? If so, what is the antidote or treatment?*

M.D., New York.

Answer.—Although patients do not often show an alarming degree of iodine sensitivity during excretory urography, the possibility of such reaction must be considered. A history of allergy should make a preliminary test imperative. Tests for sensitivity to iodine may be either oral, cutaneous, or conjunctival. The latter test, because of its simplicity, has been used more frequently. Care should be taken that the iodine solution is administered with aseptic precautions. In case there is a severe conjunctival reaction, it can usually be controlled by instilling a few drops of a 0.5% solution of cortisone. As a precautionary measure, a small amount of the contrast medium may be slowly injected intravenously and, after pausing for a few minutes, the injection may be completed. It has been claimed that a preliminary dose of acetylsalicylic acid may have prophylactic value.

SECONDARY GLAUCOMA

To the Editor:—*I would appreciate your opinion regarding medical treatment of acute glaucoma in a 60-year-old debilitated woman, who has had diabetes for 20 years. The eye is blind, with the pupil in mid-dilatation, and rubeosis iridis and retinopathy are present.*

M.D., New York.

Answer.—The secondary glaucoma caused by rubeosis iridis constitutes the most difficult problem in the management of glaucomas. There is no medical treatment of value; the pain caused by the condition commonly leads to enucleation, which is the procedure preferred. Palliative surgical therapy, such as cyclodiathermy, may be useful in controlling pain and perhaps intraocular pressure but will not restore vision. The retrobulbar injection of alcohol may also be of some value in relieving pain. If the eye is not painful, no treatment is indicated.

PROGRESSIVE MUSCULAR DYSTROPHY

To the Editor:—*For two years I have had as a patient a 32-year-old white man with progressive muscular dystrophy. He has been given therapeutic doses of vitamin B complex and vitamin C and, also, up to 40 mg. of vitamin E daily, with fair results. Is there any more promising therapy?*

Joseph G. Varkol, M.D., Clifton, N. J.

Answer.—Progressive muscular dystrophy is a disease usually beginning early in life. It occurs more frequently in males, the ratio being about 5 to 1. The disease rarely begins after 20 years of age. Often, several members of a family are affected. Progress is gradual, and the patient is usually finally bedridden. Prognosis is poor if the respiratory muscles become involved. Treatment consists of palliative measures. Favorable results to some degree have been reported with the use of vitamins, especially vitamin E, but their value is not established. There is marked loss of muscle power and tone in this

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

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disease; however, mild massage with passive resistive exercises is helpful in most cases. Inactivity and muscle disuse should be discouraged, but muscular exertion should be avoided. Back braces are of value in patients in whom scoliosis and lordosis are becoming marked. Other orthopedic appliances are useful at times. Recently, adenosine-5-monophosphate has been used, with reported success. Theoretically, this drug stimulates muscle regeneration, and it is worthy of a thorough trial in progressive muscular dystrophy. The suggested dose is 25 mg. in a gelatin base given intramuscularly daily for five days and thereafter about three times a week. Later, frequency of administration may be reduced to once or twice a week.

OCULOMOTOR PARALYSIS IN A DIABETIC

To the Editor:—*A 55-year-old man, a diabetic for many years, had an accident in which the scalp was lacerated and he momentarily "blacked out." A few days later double vision, drooping of the eyelid, and paralysis of the internal rectus developed. Is it possible that the blow to the head produced a lesion around the nucleus of the third nerve that became evident a few days later? Would it be proper to utilize vitamin B_{12} on the assumption that the patient has diabetic neuritis?* *Max J. Schroeder, M.D., New York.*

Answer.—It is impossible from the limited information given to answer this question with any degree of certainty; however, it is unlikely that a patient who sustained a blow to the head causing a laceration of the scalp and only a momentary "black-out" would, as a result, sustain a sufficiently severe injury to cause partial paralysis of the third cranial nerve a few days later with no other symptoms. Admittedly, a minor blow to the head could produce a subdural hematoma, which might result in a third nerve palsy, but if this occurred, there would certainly be other symptoms that are not listed. On the other hand, it is well known that diabetics, especially those with arteriosclerosis, often have involvement of one of the nerves to the extraocular muscles, either the third, fourth, or sixth cranial nerves. It would seem more likely that this patient had involvement of the third cranial nerve on that basis rather than as a result of this relatively minor injury. There would be no objection to the administration of vitamin B_{12} in this case but no assurance that this or any other form of therapy would prove beneficial. Involvement of the ocular motor nerves as the result of diabetes and arteriosclerosis is often temporary, and the condition frequently improves spontaneously.

CAST OF THE COLON

To the Editor:—*A 38-year-old, apparently healthy woman had abdominal discomfort and then evacuated what appeared to be a solid cast of the inner outline of the colon. A competent pathologist analyzed the cast carefully and concluded that it was composed of necrotic tissue. Are there references in the literature to similar instances?*

Max J. Schroeder, M.D., New York.

Answer.—Granting that the material passed had its source in colonic tissue, the case is unusual, owing to the mildness of the symptoms and apparent good health of the patient. Under the circumstances, one would expect the material to be the familiar mucus cast seen in patients with mucous colitis. A coating of decomposed meat tissue and other food materials on such casts could give the appearance of necrotic tissue. The medical literature of recent years cites no case report of similar nature. Volume 7 (1886) of the Index-Catalogue of the Library of the Surgeon General's office, United States Army, contains numerous references to articles on intestinal concretions and casts, but the cases reported, mostly of foreign origin, apparently are not identical to the one under consideration. Later articles dealing with membranous enteritis, enterocolitis and colitis, pseudomembranous enteritis, and necrotic and ulcerous enteritis and jejunitis, all conditions in which shreds of membrane may be passed in the stool, are invariably characterized by a stormy clinical course, sometimes with fatal termination. In Gould's and Pyles' text, Anomalies and Curiosities of Medicine (New York, Sydenham, Publishers, 1901, p. 643), a case is described in which a slough of the intestine followed intussusception.

VINCENT'S INFECTION

To the Editor:—*What is the simplest or most efficient office procedure for staining a smear for diagnosis of Vincent's infection?* *Harry L. Parker, M.D., Lockport, N. Y.*

Answer.—The simplest procedure is staining with methylrosaniline chloride (gentian violet); however, the stained smear alone is no longer considered diagnostic, since Vincent's spirochetes (Borrelia vincenti) and the fusiform organisms are normal inhabitants of the mouth. Pain, foul odor, and sloughing of the gingival tissues are characteristic signs of so-called Vincent's infection.

RAZORS AND HOMOLOGOUS SERUM HEPATITIS

To the Editor:—*My attention has been called to the query that appeared in* The Journal *Jan. 10, 1953, page 166, concerning "Razors and Homologous Serum Hepatitis." While it is true that the virus of serum hepatitis can be inactivated by ultraviolet light, recent work conducted by this laboratory, which is shortly to be published, has demonstrated that the levels of ultraviolet energy required to accomplish this are much higher than had previously been believed necessary. General statements that the virus of serum hepatitis can be inactivated by ultraviolet irradiation should therefore be made with caution and reservation. There is no evidence that the usual germicidal solutions can be relied on; in fact, what little evidence there is indicates that cresol, phenol, ether, and thimerosal (Merthiolate) are ineffective. The statement "Water sterilization at 60 to 80 C for one or two hours will kill the virus . . ." is not in keeping with our experience with the effect of heat on the agent. As reported in a paper read before the American Public Health Association in Cleveland, Oct. 23, 1952 (abstracted,* Pub. Health Rep. **68:***131, 1953), heating plasma containing the virus of serum hepatitis for 4 hours at 60 C was found ineffective. The "Minimum Requirements for Citrated Whole Blood" issued by the National Institutes of Health (ed. 3, Feb. 19, 1953) stipulates that apparatus and instruments capable of transmitting serum hepatitis from one person to another be heat-sterilized and contains the following statement: "Heat sterilization shall be by autoclaving for 30 minutes at 121.5° C. (15 lb. pressure), by dry heat for 2 hours at 170° C., or by boiling in water for 30 minutes." This is severe treatment for sharp cutting instruments, such as razors, but to recommend anything less stringent would be unwise.*

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NECROSIS OF THE FEMORAL HEAD

To the Editor:—*In* The Journal, *March 7, 1953, page 874, I note a query about "the best method for treating necrosis of the femoral head following a fracture of the hip." The answer is categorical with respect to the use of the prosthetic heads. An accumulating experience in the use of these does not seem to justify the hopes that were originally held out for them. More and more cases of failure are being seen not only in arthritic patients but also in postfracture patients. After such failures, I have used the resection angulation operation as a two stage procedure* (Surgery **13:***55, 1943) and, since 1945, as a one stage procedure* (Bull. Hosp. Joint Dis. **9:***187, 1948). The results of a follow-up study of about 50 of these patients indicate a higher percentage of satisfactory results than are obtained with the other methods* (New York State J. Med., **53:***1201, 1953).*

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